Sleep duration and nocturnal blood pressure dip

Short sleep duration is associated with blood pressure non dipping pattern in type 1 diabetes: The DIAPASOM study

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**Objective:** To assess whether nocturnal blood pressure dipping status in type 1 diabetes is correlated with specific sleep characteristics and differences in nocturnal glycaemic profiles.

**Research Design and Methods:** Twenty type 1 adult diabetic patients underwent sleep studies with simultaneous 24h ambulatory blood pressure monitoring, and continuous nocturnal glucose monitoring.

**Results:** Fifty five percent of patients exhibited blunted blood pressure dipping. They did not differ from dippers for age, BMI, systolic (SDP)/diastolic blood pressure (DBP). Total Sleep Period (TSP) was higher in dipper group (497±30 vs. 407±44 min for dippers and non dippers, respectively, p<0.001). TSP was correlated with SBP and DBP day-night differences (r=0.44 and 0.49, respectively). Periods of nocturnal hypoglycaemia (i.e. % of TSP with glycaemia <70mg/dL) were longer in dipper subjects (8.1±10.7 vs. 0.1±0.4% for dippers and non dippers, respectively, p=0.02).

**Conclusions:** Dipping status in type 1 diabetes was associated with longer sleep duration and with hypoglycaemia-unawareness.
Ambulatory blood pressure monitoring (ABPM) demonstrates during sleep a normal decline of more than 10% in blood pressure (BP) corresponding to the so-called “dipping status” (DS). In type 1 diabetes, non-dipping status (NDS) is more prevalent (1) and associated with increased risks for sustained hypertension, retinopathy, and nephropathy (1-3). Dipping pattern could be influenced by sleep duration, and associated sleep disorders (4). In type 1 diabetes, sleep stability impacts on sleep-related hypoglycaemias by changing awakening responses to these episodes (5). Our hypothesis was that type 1 diabetic subjects with more stable sleep could exhibit normal BP dip, and because of higher arousal thresholds, could present an increased frequency of nocturnal hypoglycaemias.

RESEARCH DESIGN AND METHODS

We investigated prospectively 22 unselected adult, male, type 1 diabetic patients using complete sleep studies with simultaneous 24h ABPM and nocturnal continuous blood glucose monitoring during a 24h hospitalisation. Patients suffered from type 1 diabetes according to American Diabetes Association definition. They were excluded when presenting with severe uncontrolled hypertension (Systolic BP (SBP) ≥180 and/or diastolic BP (DBP) ≥110 mmHg). Complete data were available in 20 subjects. The study was approved by our local ethic committee and registered on clinical trials database (NCT 00805974).

ABPM (Novacor®, Rueil Malmaison, France) was performed according to European recommendations (6). To differentiate daytime from nighttime BP, analysis was based on Total Sleep Period (TSP) i.e. sleep period objectively determined by electroencephalographic recordings between first sleep onset and final awakening.

Overnight polysomnography recorded sleep and respiratory events according to standard criteria. Sleep apnoea syndrome was defined when Apnoea-Hypopnoea Index (AHI), i.e. number of apnoea plus hypopnoea per hour, was above 15 events/h (7).

Continuous glucose monitoring system (Medtronic, Minneapolis, USA) consisted of a subcutaneous glucose-sensing device with good correlation between blood and subcutaneous glucose measurements (8). A glycaemia upper 150 mg/dL was considered as hyperglycaemia. Hypoglycaemia was defined as glucose level below 70 mg/dL (9).

Quality of life was determined using Diabetes Quality of Life (DQOL) questionnaire, as implemented during the DCCT trial (10).

Statistical analysis: Variables were described by mean and standard deviation or by frequency distribution. Normality was analysed by Skewness and Kurtosis tests. Comparisons were made using Student or Mann-Whitney test, depending on normality of distribution. For discrete variables, Chi square was used. Correlation between (i) TSP and day-night SBP or DBP, (ii) Heart rate (HR), TSP and total sleep time, used Pearson correlation since data followed normal distribution. Spearman correlation was used between HR and nocturnal hypoglycaemias since data were not normally distributed (NCSS software 1997, US, Kaysville, Utah).

RESULTS

Nine dipper and 11 non dipper subjects were identified. The two groups did not differ in terms of anthropometrics (Age 47±12 years, Body Mass Index 26.7±3.2 kg/m²), diabetes characteristics (HbA1c 8±1%, disease duration 22±10 years, plasma creatinine 87±18 µmol/L, urinary albumin excretion 32±32 µg/min) and 24 hours mean SBP (121±17 mmHg), DBP (79±9 mmHg) and HR (71±13 beats/min).
Fifty five percents of subjects exhibited an obstructive sleep apnoea syndrome (AHI 22.6±18.2 events/hour) without difference in terms of prevalence and severity between dipper and non dippers. TSP as well as Total Sleep Time (TST), i.e. the sum of all sleep periods assessed by EEG, were significantly higher in dipper patients (TSP 497±30 and 407±44 min, p<0.001, TST 425±82 and 356±72 min, p=0.03, for dippers and non dippers, respectively). Sleep architecture tended to demonstrate more stages 1-2, less stages 3-4 and Rapid Eye Movement (REM) in non dipper patients (Stage 1-2 65±7 and 71±14%, Stage 3-4 13±6 and 9±8%, REM 22±4 and 20±7% for dippers and non dippers, respectively). SBP and DBP day-night differences were significantly correlated with TSP (r=0.44 and r=0.49 for SBP and DBP differences, respectively) (Figure 1).

Nocturnal hypoglycaemias were more frequent among dipper subjects (8.1±10.7 and 0.1±0.4% of sleep time spent in hypoglycaemia for dippers and non dippers, respectively, p=0.02). DQOL was significantly impaired in non dipper subjects only for the treatment satisfaction item (82.2±13.5 vs. 63.7±19.3 for Dippers and Non dippers, respectively, p=0.03).

Nocturnal mean HR was negatively correlated with TSP (r = -0.53), TST (r = -0.44) and time spent in hypoglycaemia (r = -0.56).

CONCLUSION
Sleep recordings, BP measurements and continuous glucose monitoring were used together in type 1 diabetic patients. Such a complexity explains the relatively limited sample of patients included. Polysomnography allowed defining objectively the beginning and end of sleep and then an appropriate classification of dippers and non-dippers (11).

To our knowledge, no study has explored the potential link between abnormal nocturnal BP pattern and altered sleep quality in type 1 diabetes. In our work, shorter sleep duration explained 19% to 24% of the decrease in day-night BP difference (r²=0.19 and 0.24 for SBP and DBP, respectively), and 28% of the increase of HR (r²=0.28). Outside the scope of type 1 diabetes, general population studies have demonstrated that short sleep duration habits were associated with increased risk of developing hypertension (12).

We found a high prevalence of sleep apnoea among our type 1 diabetic subjects. Although sleep apnoea is clearly related to non dipping BP pattern (13), it was not an independent explaining factor for non dipping in our population.

Hypoglycaemia-unawareness during the night in type 1 diabetic patients is a major concern in disease management. Indeed, convulsions, neurologic after effects, and “dead-in-bed” syndrome have been reported in this condition (14). Subjects fail to awake when hypoglycaemia occurs at night, in relation with blunted counter-regulatory epinephrine level (5). Others studies suggested that unperceived hypoglycaemias occurred in patients with more efficient and more stage 3-4 sleep, without sympathetic activation (15). In our work, patients with DS, longer sleep duration and lower HR presented more unperceived hypoglycaemias. A more stable sleep which is associated to a lower sympathetic activation could explain these events.

Our study suggests that assessing sleep duration is fully relevant in clinical practice. BP non dipping status should receive particular attention in type 1 diabetic patients with short sleep duration, and hypoglycaemia-unawareness deserves a careful prevention in patients with longer and more stable sleep.

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REFERENCES
Figure 1: Sleep characteristics related to blood pressure dipping status.

Left: Total Sleep Time and sleep architecture in dipper and non dipper type 1 diabetic patients. Total Sleep Time (TST) was shorter in non dipper subjects. TST data are Mean ± Standard Deviation.*p<0.05.

Right: Positive correlation between Total Sleep Period (TSP) and day-night Systolic Blood Pressure differences (SBP).