Short Sleep Duration Is Associated With a Blood Pressure Nondipping 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 glycemic profiles.

RESEARCH DESIGN AND METHODS — Twenty type 1 diabetic adult patients underwent sleep studies with simultaneous 24-h ambulatory blood pressure monitoring and continuous nocturnal glucose monitoring.

RESULTS — Altogether, 55% of patients exhibited blunted blood pressure dipping. They did not differ from the dipper group in age, BMI, or systolic (SBP) and diastolic (DBP) blood pressure. Total sleep period (TSP) was higher in the dipper group (497 ± 30 vs. 407 ± 44 min for dippers and nondippers, respectively, $P < 0.001$). TSP was correlated with SBP and DBP day-night differences ($r = 0.44$ and 0.49, respectively). Periods of nocturnal hypoglycemia (i.e., % of TSP with glycemia <70 mg/dl) were longer in the dipper group (8.1 ± 10.7 vs. 0.1 ± 0.4% for dippers and nondippers, respectively, $P = 0.02$).

CONCLUSIONS — Dipping status in type 1 diabetes was associated with longer sleep duration and with hypoglycemia unawareness.

Diabetes Care 32:1713–1715, 2009

During sleep, ambulatory blood pressure monitoring (ABPM) demonstrates a normal decline of over 10% in blood pressure (BP), corresponding to the so-called dipping status. In type 1 diabetes, nondipping status is more prevalent (1) and is 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 sleep-related hypoglycemia 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 hypoglycemia.

RESEARCH DESIGN AND METHODS

— We prospectively investigated 22 unselected adult, male, type 1 diabetic patients who completed sleep studies with simultaneous 24-h ABPM and nocturnal continuous blood glucose monitoring during a 24-h hospitalization. Patients suffered from type 1 diabetes according to American Diabetes Association criteria. Patients presenting with severe uncontrolled hypertension (systolic BP [SBP] ≥180 mmHg and/or diastolic BP [DBP] ≥110 mmHg) were excluded. Complete data were available for 20 patients. The study was approved by our local ethics committee and registered in a clinical trials database.

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 apnea syndrome was defined when apnea-hypopnea index (AHI), i.e., number of apnea plus hypopnea per hour, was above 15 events/h (7).

Continuous glucose monitoring (Medtronic, Minneapolis, MN) consisted of a subcutaneous glucose-sensing device with good correlation between blood and subcutaneous glucose measurements (8). A glucose level >150 mg/dl was considered hyperglycemia, and a glucose level <70 mg/dl was considered hypoglycemia (9).

Quality of life was determined using the diabetes quality of life (DQOL) questionnaire, as implemented during the Diabetes Control and Complications Trial (10).

Statistical analysis

Variables were described by mean and SD or by frequency distribution. Normality was analyzed by skewness and kurtosis tests. Comparisons were made using Student's *t* or Mann-Whitney tests, depend-

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Received 4 March 2009 and accepted 5 June 2009.
Published ahead of print at http://care.diabetesjournals.org on 19 June 2009. DOI: 10.2337/dc09-0422. Clinical trial reg. no. NCT00805974, clinicaltrials.gov.
J.-L.P. and J.-M.M. contributed equally to this work.

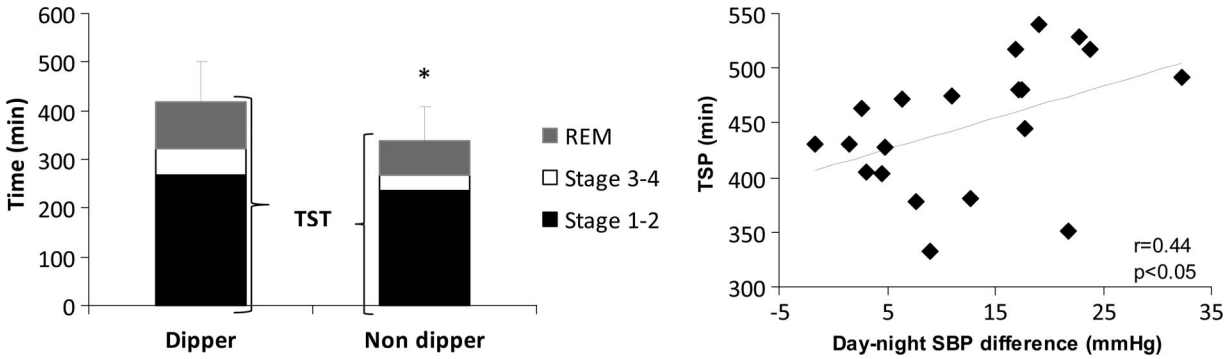

Figure 1—*Sleep characteristics related to BP dipping status.* Left*: TST and sleep architecture in dipper and nondipper type 1 diabetic patients. TST was shorter in nondipper subjects. TST data are mean + SD.* *P < *0.05.* Right*: Positive correlation between TSP and day-night SBP differences.*

ing on normality of distribution. For discrete variables, χ^2 was used. Correlation between *1*) TSP and day-night SBP or DBP and *2*) heart rate (HR), TSP, and total sleep time (TST) was determined using Pearson correlations, since data followed normal distribution. Spearman correlations were used between HR and nocturnal hypoglycemia, since data were not normally distributed (NCSS statistical software 1997; NCSS, Kaysville, UT).

RESULTS — Of the 20 participants, 9 dipper and 11 nondipper subjects were identified. The two groups did not differ in terms of anthropometrics (age 47 ± 12 years, BMI 26.7 ± 3.2 kg/m^2), diabetes characteristics (A1C 8 ± 1%, disease duration 22 ± 10 years, plasma creatinine 87 ± 18 μmol/l, urinary albumin excretion 32 ± 32 μg/min), and 24-h mean SBP (121 ± 17 mmHg), DBP (79 ± 9 mmHg), and HR (71 ± 13 bpm).

Fifty-five percent of subjects exhibited an obstructive sleep apnea syndrome (AHI 22.6 ± 18.2 events/h) without difference in terms of prevalence and severity between dippers and nondippers. TSP and TST, i.e., the sum of all sleep periods assessed by electroencephalogram, 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 nondippers, respectively). Sleep architecture tended to demonstrate more stages 1–2 and less stages 3–4 and rapid eye movement (REM) in nondipper 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 nondippers, respectively, NS). SBP and DBP day-night differences were significantly correlated with TSP ($r = 0.44$ and $r = 0.49$ for SBP and DBP differences, respectively) (Fig. 1).

Nocturnal hypoglycemia was more frequent among dipper subjects (8.1 ± 10.7 and 0.1 ± 0.4% of sleep time spent in hypoglycemia for dippers and nondippers, respectively, $P = 0.02$). DQOL was significantly impaired in nondipper subjects only for the treatment satisfaction item (82.2 ± 13.5 vs. 63.7 ± 19.3 for dippers and nondippers, respectively, $P = 0.03$).

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

CONCLUSIONS — 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 for objectively defining the beginning and end of sleep and then an appropriate classification for dippers and nondippers (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 19–24% of the decrease in day-night BP difference ($r^2 = 0.19$ and 0.24 for SBP and DBP, respectively) and 28% of the increase in HR ($r^2 = 0.28$). 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 apnea among our type 1 diabetic subjects. Although sleep apnea is clearly related to nondipping BP pattern (13), it was not an independent explaining factor for nondipping in our population.

Hypoglycemia unawareness during the night in type 1 diabetic patients is a major concern in disease management. Indeed, convulsions, neurologic aftereffects, and "dead-in-bed" syndrome have been reported in this condition (14). Subjects fail to awake when hypoglycemia occurs at night, in relation with blunted counterregulatory epinephrine level (5). Other studies suggest that unperceived hypoglycemia occurred in patients with more efficient and more stage 3–4 sleep, without sympathetic activation (15). In our work, patients with dipping status, longer sleep duration, and lower HR presented more unperceived hypoglycemia. A more stable sleep, which is associated with a lower sympathetic activation, could explain these events.

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

Acknowledgments— We thank the Direction de la Recherche Clinique of Grenoble University Hospital for the financial contribution that funded this study.

No potential conflicts of interest relevant to this article were reported.

Nathalie Arnol, Hélène Pierre, and Sandrine Mouret, clinical research assistants and statistical specialists, greatly contributed to this work.

References

1. Dost A, Klinkert C, Kapellen T, Lemmer A, Naeke A, Grabert M, Kreuder J, Holl RW. Arterial hypertension determined by ambulatory blood pressure profiles: contribution to microalbuminuria risk in a multicenter investigation in 2,105 children and adolescents with type 1 diabetes. Diabetes Care 2008;31:720–725

2. Benhamou PY, Halimi S, De Gaudemaris R, Boizel R, Pitiot M, Siche JP, Bachelot I, Mallion JM. Early disturbances of ambulatory blood pressure load in normotensive type 1 diabetic patients with microalbuminuria. Diabetes Care 1992; 15:1614–1619
3. Stella P, Tabak AG, Zgibor JC, Orchard TJ. Late diabetes complications and nondipping phenomenon in patients with type 1 diabetes. Diabetes Res Clin Pract 2006;71:14–20
4. Matthews KA, Kamarck TW, H Hall M, Strollo PJ, Owens JF, Buysse DJ, Lee L, Reis SE. Blood pressure dipping and sleep disturbance in African-American and Caucasian men and women. Am J Hypertens 2008;21:826–831
5. Schultes B, Jauch-Chara K, Gais S, Hallschmid M, Reiprich E, Kern W, Oltmanns KM, Peters A, Fehm HL, Born J. Defective awakening response to nocturnal hypoglycemia in patients with type 1 diabetes mellitus. PLoS Med 2007;4:e69
6. O'Brien E, Asmar R, Beilin L, Imai Y, Mallion JM, Mancia G, Mengden T, Myers M, Padfield P, Palatini P, Parati G, Pickering T, Redon J, Staessen J, Stergiou G, Verdecchia P. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. J Hypertens 2003;21:821–848
7. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research: the report of an American Academy of Sleep Medicine Task Force. Sleep 1999;22:667–689
8. Rebrin K, Steil GM, van Antwerp WP, Mastrototaro JJ. Subcutaneous glucose predicts plasma glucose independent of insulin: implications for continuous monitoring. Am J Physiol 1999;277:E561–E571
9. Tamborlane WV, Beck RW, Bode BW, Buckingham B, Chase HP, Clemons R, Fiallo-Scharer R, Fox LA, Gilliam LK, Hirsch IB, Huang ES, Kollman C, Kowalski AJ, Laffel L, Lawrence JM, Lee J, Mauras N, O'Grady M, Ruedy KJ, Tansey M, Tsalikian E, Weinzimer S, Wilson DM, Wolpert H, Wysocki T, Xing D. Continuous glucose monitoring and intensive treatment of type 1 diabetes. N Engl J Med 2008;359:1464–1476
10. Reliability and validity of a diabetes quality-of-life measure for the diabetes control and complications trial (DCCT): the DCCT Research Group. Diabetes Care 1988;11:725–732
11. Fagard RH, Staessen JA, Thijs L. Optimal definition of daytime and night-time blood pressure. Blood Press Monit 1997; 2:315–321
12. Gangwisch JE, Heymsfield SB, Boden-Albala B, Buijs RM, Kreier F, Pickering TG, Rundle AG, Zammit GK, Malaspina D. Short sleep duration as a risk factor for hypertension: analyses of the first National Health and Nutrition Examination Survey. Hypertension 2006;47: 833–839
13. Ziegler MG. Sleep disorders and the failure to lower nocturnal blood pressure. Curr Opin Nephrol Hypertens 2003;12: 97–102
14. Tu E, Twigg SM, Semsarian C. Sudden death in type 1 diabetes: the mystery of the 'dead in bed' syndrome. Int J Cardiol. 1 August 2008 [Epub ahead of print]
15. Pillar G, Schuscheim G, Weiss R, Malhotra A, McCowen KC, Shlitner A, Peled N, Shehadeh N. Interactions between hypoglycemia and sleep architecture in children with type 1 diabetes mellitus. J Pediatr 2003;142:163–168