

Obstructive Sleep Apnea Syndrome in Type 2 Diabetes Mellitus, Case Report and Review of Literature

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Abstract

Humans spend almost 33% of their life sleeping, therefore, poor sleep quality can have both short-term and long-term consequences on an individual's quality of life. Obstructive sleep apnea syndrome (OSA) is the most common sleep disorder characterized by respiratory cessation for at least 10 seconds, associated with a decreased oxygen saturation. OSA is a risk factor for heart rhythm disorders. The presence of heart rhythm disorders correlates with the severity of OSA, especially in middle-aged patients with type 2 diabetes mellitus (DM). The metabolic consequences of OSA contribute to a general imbalance. When circadian rest and activity rhythms are disrupted, hormonal and metabolic regulations also become desynchronized. OSA has an important role in the development of insulin resistance, increased diabetes risk and altered glycemic control in patients with type 2 DM. Taking into account that OSA is an independent risk factor that

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contributes to the appearance and the progression of diabetes complications, we aimed to present the case of a male patient with type 2 diabetes, aged 70 years old in whom the diagnosis of OSA was established using nocturnal polysomnography. Furthermore, in order to demonstrate the relationships between OSA, poor diabetes control and cardiovascular risk, during polysomnography Holter monitoring and continuous glucose monitoring was also performed.

Keywords: Sleep apnea; Type 2 diabetes; Obesity; Cardiovascular risk; Arrhythmia.

Introduction

The increase in prevalence of obesity has become a worldwide major health problem, with a psychological impact that can affect the quality of life. Many chronic conditions are directly caused or adversely affected by obesity. In 2014, there were 1.9 billion adults (39%) over the age of 18 with overweight and about 600 million adults (13%) with obesity. Obese patients are more likely to develop obstructive sleep apnea (OSA) or to have a severe form of OSA than people with normal weight, and prevalence of OSA is increasing worldwide because of the ongoing obesity epidemic [1]. Weight loss may be an effective therapy and has been shown to reduce the severity of symptoms of OSA and sometimes, to its complete resolution. Weight loss may also make some changes in insulin resistance, cholesterol endothelial function and inflammatory markers [2]. OSA is a condition characterized by recurrent episodes of obstruction of the upper airway leading to sleep fragmentation and intermittent hypoxia during sleep [3].

The relative risk of developing type 2 diabetes increases steeply with increasing body mass index (BMI). Hyperglycemia, insulin resistance and excess fatty acids increase oxidative stress, disrupt protein kinase C signaling and can lead to vasoconstriction, thrombosis, atherogenesis [4]. A frequent comorbidity in patients with type 2 diabetes

is OSA which is characterized by repetitive upper airway collapse during sleep, accompanied by recurrent oxygen desaturations, nocturnal arousal, and fragmented sleep. It is estimated that OSA affects nearly 1 billion people worldwide. 9% of women and 24% of men in the 30-60 age group have OSA. 4% of women and 9% of men have moderate and severe forms [5]. More than 50% of the patients with diabetes have OSA which is associated with coronary and cerebral vascular disease, and it can affect cardiovascular structure and function by several distinct mechanisms such as intermittent hypoxia, sleep fragmentation, and intrathoracic pressure swings [6].

OSA is a frequent comorbidity in patients with type 2 diabetes and an independent risk factor for cardiovascular disease. OSA patients are more likely than non-OSA patients to develop type 2 diabetes, while more than half of patients with type 2 diabetes suffer from OSA. OSA has been linked to the development of incident type 2 diabetes [7]. Intermittent hypoxia and fragmentation of sleep, the two major features of apnea, lead to disorders of glucose metabolism, mainly by activating the nervous system and the hypothalamic-pituitary axis and changes in the inflammatory pathways. Other possible mechanisms include hypoxic damage to the pancreas and changes in the hypothalamic pathway to control glucose. Studies strongly suggest an association

between apnea - insulin resistance and apnea - glucose intolerance [8].

Repetitive obstructive apneas expose the heart and circulation to a cascade of noxious stimuli that may initiate a cardiovascular disorder. Patients with moderate to severe OSA have a 2.9-fold higher risk of developing high blood pressure, and 50% of those with cardiovascular disease have concomitant OSA [9]. In addition, all kinds of arrhythmias have been observed in patients with sleep apnea ranging from asymptomatic sinus bradycardia to sudden cardiac death [10].

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Aim

In our case report, we evidence the relationships between OSA and type 2 diabetes with chronic complication. Furthermore, we highlight the importance of nocturnal polysomnography in patients with diabetes and obesity at risk for OSA, as well as the importance of a thorough investigation of the cardiovascular diseases in these patients.

Case report

A case of a 70 year Caucasian man, BMI=34.8 kg/m², diagnosed with diabetes since 2007, initially in treatment with oral anti-diabetic drugs (OAD) for 5 years. Afterwards, due to poorly controlled diabetes and the appearance of micro and macrovascular complications, insulin therapy was initiated. Currently, the patient, presented with polyuria, polydipsia, fatigue to minimum effort and daily somnolence, as well as snoring during sleep.

The patient was included in a therapeutic educational program in order to acquire the

necessary knowledge for self-monitoring of blood glucose for fasting, preprandial and 1h and 2 h postprandial values and recording the values in a logbook, as well as knowledge regarding nutritional medical therapy and decision-making relating food choices.

Considering the serious general condition of the patient, in order to elucidate the diagnosis, in collaboration with the cardiologist and pneumologist it was decided to perform Holter monitoring and continuous glucose monitoring (CGM), concomitant with the respiratory polysomnography recording.

Nocturnal polysomnography was performed. This is a continuous recording during night of several parameters: nasal airflow, thoracic and abdominal movements, heart rate and oxygen saturation, the number of snores and changes in body position during sleep [23]. The apnea/hypopnea index (AHI) was defined as the number of apnea/hypopnea events divided by the total sleep time and expressed by the number of events per hour. Severity of OSA was classified as normal/mild: AHI <15/hr, moderate AHI 15-30 and severe AHI >30. Furthermore, concomitantly with polysomnography registration, a Holter monitoring was performed, in order to evaluate whether possible hypoxic events were also related to arrhythmic events, as well as a CGM registration over 8 hours. The nocturnal polysomnography illustrated that the patient suffered from severe OSA based on the fact that he had a high score of AHI >30 (53.5-detected value), multiple episodes of apnea (29 per hour) and hypopnea (24.5 per hour). The longest apnea was about 1 minute, and the longest hypopnea was about 53 seconds (Table 1).

Respiratory evaluation	Findings
AHI (Desat.-Cor.) (Per hour)	53.5
RDI (Desat.-Cor.) (Per hour)	53.5
Apnea Index AI (Desat.-Cor.) (Per hour)	29
Hypopnea Index HI (Desat.-Cor.) (Per hour)	24.5
No. of Apnea	153
Mean duration of apneas (Sec)	26
Longest Apnea (Min) t=03:02:09	01:00
Apnea/ Hypopnea time per hour (Min per hour)	20:11
Longest hypopnea (Sec) t=00:50:05	53
No. of hypopnea (n)	129

Table 1: Respiratory events registered on polysomnography where apnea and hypopnea episodes are quantified according to their duration and number per hour.

In this case, we observed multiple episodes of obstructive sleep apnea (144 episodes) as well as an episode of central apnea, resulting in the diagnosis of mixt sleep apnea, mainly

obstructive. The central episode lasted 10-14,9 seconds and the majority of the episodes of obstructive sleep apnea lasted more than 20 seconds (Table 2).

	Central	Obstructive	Mixt
Number	1	144	8
Longest duration	13 sec	1 min	50 sec
Duration < 10 sec (%)	0	0	0
Duration 10-14,9 sec (%)	100	20	25
Duration 15-20 sec (%)	0	12	12
Duration >20 sec (%)1	0	68	62

Table 2: The distribution of central, obstructive, and mixt apnea episodes evidenced on polysomnography, recorded as number and duration.

SpO₂/Pulse registered on polysomnography showed a number of desaturations of 423, corresponding to 2:34 hours of desaturation, the longest one being 1:19 minute and the

lowest SpO₂ 52%. OSA has an important influence on the heart rate therefore in our case we report an oscillation of pulse, with a minimum value of 25 beats per minute (bpm) and a maximum value of 211 bpm (Table 3).

Evaluation of SpO ₂ /Pulse	Findings
Desaturation Index DI (per hour)	58,4
No. of desaturations (n)	423
No of desaturations < 90% (n)	365
Total time (Hrs)	02:34:03
Time per hour (Min per hour)	21:17
Lowest Desaturation (%) 02:05:04	52
Longest desaturation (min) 03:40:57	01:19
Max Saturation (%) 22:03:26	96
Min Saturation (%) 04:55:08	50
T90 (%)	37
Min. pulse 00:59:2 (1/min)	25
Max. pulse 04:58:21 (1/min)	211

Table 3: SpO₂/Pulse evaluation on polysomnography.

Furthermore, we observed that position during sleep had the greatest impact when the patient slept on the back (82% of the time), therefore most episodes of

apnea/hypopnea, desaturation and snoring occurred during this time and position (Table 4). The recordings of these events is presented in Figure 1.

Position	Upright	Right	Back
Time (time slice)	1:15:01 Hrs (16%)	11 :45 min (2%)	6:32:51 Hrs (82%)
Apneas (number)	0	8	145
(Apneas %)	0%	-5%	-95%
Central Apnea (number)	0	0	1
Obstructive Apnea (number)	0	7	137
Mixt Apnea	0	1	7
Hypopnea	16	6	107
AHI (relate to pos. time)	13	71	38
AHI (relate to total time)	3	3	48
Desaturation (number)	56	8	359
Snoring (number)	0	9	127

Table 4: Respiratory events recorded on polysomnography, influenced by position during sleep.

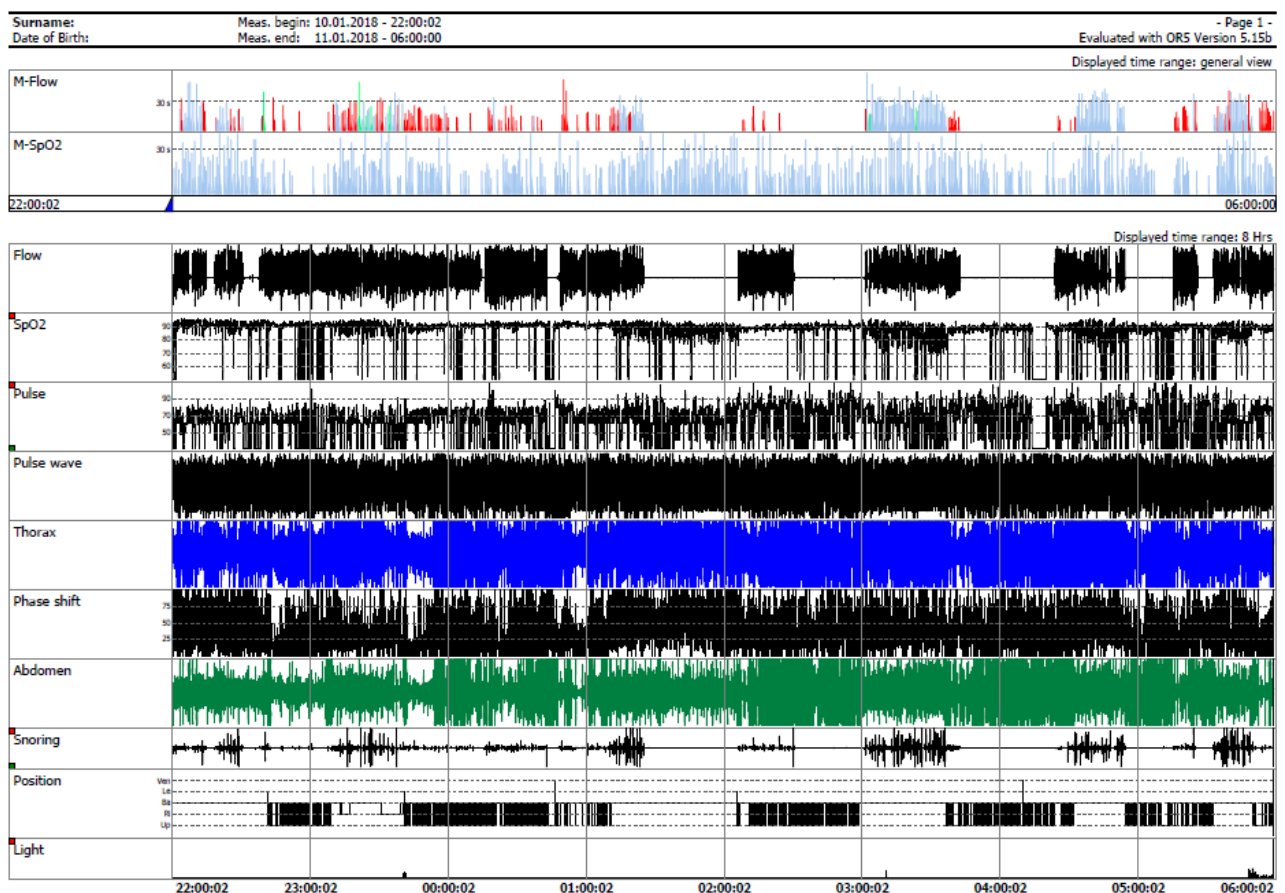


Figure 1: Nocturnal polysomnography registration.

For the CGM recoding, we used a professional CGM system (CGMS) device which does not allow data to be made available directly to patients in real time, but provides data that will be available for review by physicians after the recording interval (up to 144 hours). The patient received detailed instructions on wearing the sensor, study compliance, meter

use and maintaining a log sheet. Before the sensor was set up, the patient was asked about sleeping position and about his normal daily routine. We performed CGMS for 8 hours, in the same time with polygraphy and we evaluated fluctuations of glycemic values, minimum value was 191 mg/dl and highest value 222 mg/dl (Figure 2).

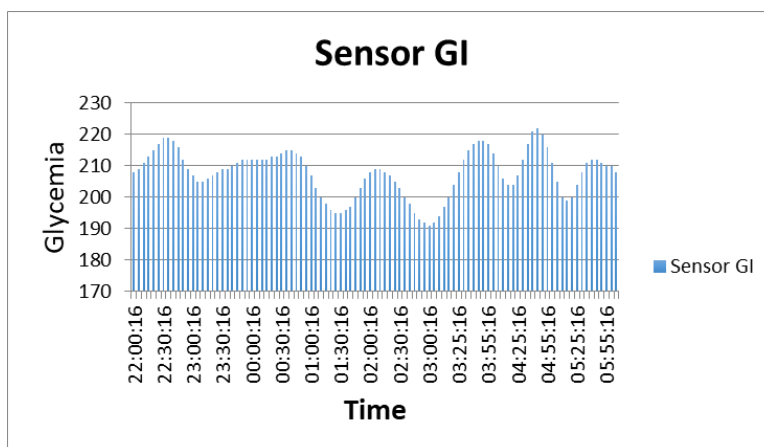


Figure 2: Continuous glucose monitoring over 8 hours.

The 24-hour Holter monitor highlighted the following data: multiple pauses R-R longer than 6 seconds (max 12 seconds), during the night. Atrial fibrillation was registered throughout monitoring with minimum ventricular rate 19 beats per minute,

maximum ventricular rate 148 beats per minute, average ventricular rate 76 beats per minute. Following the results acquired by holter monitoring (Figure 3), the patient was referred to permanent cardiostimulation type VVI, a procedure without complications, with a favorable evolution.

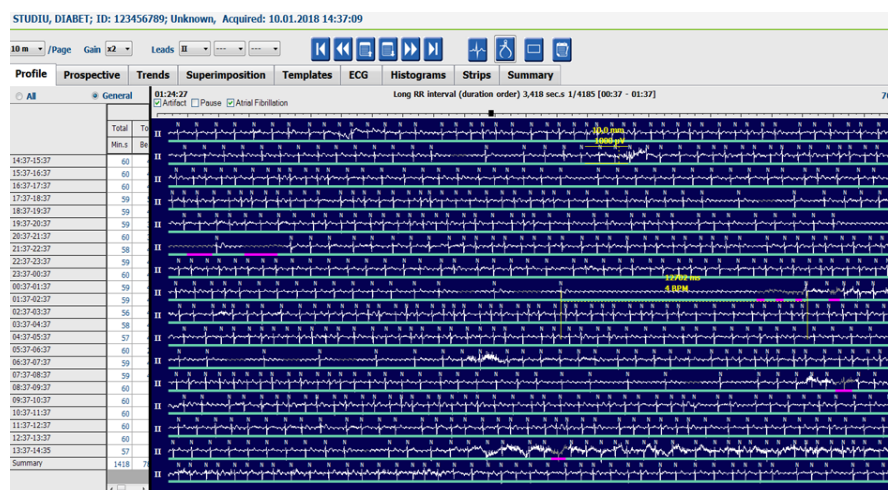


Figure 3: 24 hours Holter monitoring.

Discussions and Conclusions

Intermittent hypoxia and fragmentation of sleep, the two major features of apnea, lead to disorders of glucose metabolism, mainly by activating the nervous system and the hypothalamic-pituitary axis and changes in the inflammatory pathways. Other possible mechanisms include hypoxic damage to the pancreas and changes in the hypothalamic pathway to control glucose [8].

The literature describes multiple cases of OSA in patients with type 2 diabetes and obesity, identified along with evolution of multiple complications in diabetes mellitus. The most important thing for achieving good management is a well-informed multidisciplinary team. In the case we presented, there was good collaboration between the diabetologist, cardiologist and pneumologist, about the need for frequent consultations, assistance with the treatment plan, and counseling of the patient on the benefits of a balanced diet and risks of abnormal glycemic values.

This case is a typical example of a silent evolution of type 2 DM with numerous macro and microvascular complications as diabetic neuropathy, retinopathy, peripheral arterial disease, and coronary disease. As a consequence of poorly controlled diabetes in association with obesity, sleep apnea syndrome has gradually set in with repeated episodes of partial or complete obstruction of the upper airways during sleep.

The overall prevalence of OSA diagnosed by full polysomnography in patients with type 2 DM is approximately 71% based on the average of data from five studies including a total number of nearly 1200 patients with type 2 DM. The highest estimate of 86% was reported in patients with both obesity and

diabetets enrolled in the multi-center Sleep AHEAD study [12].

Several population and clinic-based studies as Sleep Heart Health Study have assessed the prevalence and incidence of type 2 diabetes in OSA. In another study from 2010 by Aronsohn et. al., OSA prevalence was found to be 76%. The majority of these studies have used validated diabetes definitions based on fasting glucose or 2 h post-challenge glucose levels, while a few studies relied on self-reported diabetes and/or antidiabetic medication use [8].

For the proper interpretation of the case, it was decided to install CGMS simultaneously with the polysomnography evaluation in order to correlate the glycemi values with episodes of hypopnea / apnea for a period of 8 hours.

Following the interpretation of the results of the investigations, the following conclusions were reached: sever OSA was identified together with heart rhythm disorders (113 episodes of ectopic supraventricular activity, of which 3 episodes of supraventricular bigeminism and 1 episode of supraventricular tachycardia), in the presence of inadequate glycemic control, leading to arguments about the need to start appropriate therapy to slow the progression of cardio-metabolic complications.

The patient was advised to optimize his lifestyle by losing weight, making a commitment to managing his diabetes, keeping his blood pressure under control, to schedule regular physicals, pay attention to his feet all of which contribute to the improvement of OSA, Diabetes and cardiovascular risk.

Furthermore, after the patient's evaluation, we concluded that in the case we presented,

neurocognitive impairments have been linked to poor sleep. What is more, severe OSA might have contributed to the poor control of diabetes. Instability of glycemic control can also affect the evolution of cardiovascular disease and OSA, entering thus a vicious circle.

Taking into consideration the case presented and knowing that obesity and OSA are important risk factors for arrhythmias, non-fatal or fatal ischemic cardiovascular events, we recommend that patients with type 2 DM and obesity should be referred to both pneumologist for OSA screening and cardiologist for a thorough investigation in order to prevent cardiovascular events.

Conflict of interest

The authors have no conflict to disclose.

Author Contributions

Conceptualization, D.C.P.T, I.M.V., M.M., M.F. methodology, T.C., M.C.F, D.I.D., C.M.M., A.M.G.; software, M.B.G., E.N.M., R.M.M; validation, I.M.V., A.D.G., M.F., I.C.E.; formal analysis, T.G, R.M.M, I.C.E., S.M.; investigation, E.N.M, R.M.M., A.M.G, F.L.F, C.M.M; resources, M.C.F, A.D., F.M.B., F.L.F., D.C; data curation, M.M., I.M.V., I.C.E., D.I.D; writing—original draft preparation, E.N.M, R.M.M., A.M.G, F.M.B., M.B.G., C.M.M; writing—review and editing, I.M.V., A.D.G, M.F., M.M.F., M.C.F.; visualization, D.C.P.T., I.C.E., M.M.; supervision, M.M., M.F., T.G., I.M.V.; project administration, M.C.F, I.M.V, M.F., D.I.D. All authors have read and agreed to the published version of the manuscript and thus share first authorship.

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