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## THE DIFFERENCES IN SLEEP PROFILE CHANGES UNDER CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) THERAPY BETWEEN NON-OBESE, OBESE AND SEVERELY OBESE SLEEP APNEA PATIENTS

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Sleep disturbances in obstructive sleep apnea are caused mainly by repetitive apneas and hypopneas. An alternative factor contributing to disordered sleep may be the obesity, which is frequently associated with sleep apnea. The sleep disturbing effect of obesity was found previously in obese nonapneic subjects. The aim of this study was to evaluate the effect of obesity on sleep quality in sleep apnea patients in particular in patients under continuous positive airway pressure (CPAP) with successfully normalized respiration. We reviewed the archive data of 18 non-obese, 18 obese and 17 severely obese age and gender matched sleep apnea patients treated with CPAP. The polysomnographic parameters from the diagnostic night, from the second night under CPAP and from the follow up night (after three months of CPAP use) were compared. Before CPAP the apnea hypopnea index was worse in obese and in severely obese group and it normalised under CPAP in all groups. The severely obese group showed more light sleep and less REM sleep before CPAP and inversely - less light and more REM sleep in the second night under CPAP than the non-obese group. In the follow up, there was no differences in sleep profile between groups. This study indicates obesity does not affect the sleep independently of respiratory disorders. Before therapy it is associated with more severe sleep apnea and indirectly with worse sleep quality.

**Key words:** *continuous positive airway pressure, obesity, obstructive sleep apnea, polysomnography, sleep quality*

### INTRODUCTION

One of the hallmarks of the obstructive sleep apnea (OSA) is the disordered nocturnal sleep. Polysomnographic data of OSA patients include increased arousals, nocturnal awakenings and light sleep (1, 2) as well as decreased sleep efficiency (SE), REM and slow wave sleep (N3). Disordered nocturnal sleep results in daytime sleepiness and poor performance and contributes to cardiovascular consequences of OSA (3). The main cause of sleep disturbances in OSA are repetitive apneas and hyponeas with its' sleep fragmenting effect (1). Obesity as the strongest risk factor of OSA (4) affects therefore indirectly the sleep quality. However, it can also worsen the sleep directly *i.e.* independently of apneas and hypopneas. This direct association between obesity and sleep disruption was documented by Magee *et al.* (5) who described short sleep in a large cohort (over 40,000) of obese subjects as well as by Vgontzas *et al.* (6) and Resta *et al.* (7) who observed prolonged sleep onset latency (SOL), decreased SE and REM sleep, as well as increased arousal index and light sleep in the cohort of obese subjects without apneas and hypopneas. The arousing effect of tumor necrosis factor- $\alpha$  and interleukin-6 which are elevated in serum of the obesese is the probable background of these polysomnographic findings. Other possible cause is the obesity-related decrease in the

nocturnal physiologic peak of melatonin and leptin with resulting disorder of the circadian rhythm (8-10). Additionally, the sleep can be also disturbed by depression which frequently affects the obese patients. In the study of Dixon *et al.* (11) the BDI (Beck Depressions Inventory) of 487 obese patients correlated with their BMI and the surgically induced weight loss correlated with improvement in BDI.

This detrimental direct effect of obesity on sleep quality has been up to now documented in nonapneic subjects. In this study we analyzed it for the first time (except the publication of the preliminary data of this study which included smaller sample without females and without some of the present statistical analysis) (12) in OSA patients before and during continuous positive airway pressure (CPAP) therapy.

We expected that this direct effect of obesity on sleep is in untreated OSA overshadowed by the well known indirect effect *i.e.* by severe sleep fragmentation caused by apneas and hypopneas which are by far more abundant in obese patients. We expected further, that the direct effect becomes more visible after normalization of the nocturnal breathing with CPAP. The significance of the worsening of sleep quality by obesity is that it may decrease the quality of life of OSA patients under CPAP and may contribute to the previously reported persistent daytime sleepiness despite successful normalization of the nocturnal breathing in some patients (13, 14).

## MATERIAL AND METHODS

### Patients

We reviewed the archive data of OSA patients who were treated with CPAP between June 2002 and June 2005 in sleep centre of the Hospital Kuchwald, Chemnitz, Germany. The study was performed according to the Declaration of Helsinki of 1975 for Human Research and the protocol was approved by a local Ethics Committee. We included data of patients who were of age 18 or older, fulfilled the criteria of OSA (15) and were successfully normalized under CPAP regarding their nocturnal respiration (Apnea Hypopnea Index, AHI less than 10 at follow up). Exclusion criteria were mean CPAP use shorter than three hours per night (recorded by the counter in the device) and the presence of any sleep co-disturbing condition, such as periodic limb movement in sleep or narcolepsy. The design of the study included comparison of three patients groups: the non-obese (NG), the obese (OG) and the severely obese (SOG) OSA patients. Patients were assigned to these groups according to their BMI, with non-obesity ranging from 18 to 25, obesity from 30 to 40 and severe obesity from 40 upward ( $\text{kg}/\text{m}^2$ ) (16). According to epidemiological studies linking strongly OSA to obesity (4), we expected the non-obese OSA patients would be the smallest group. Therefore, the selection process began with identifying patients eligible for the non-obese group (NG). After this, patients for the presumably second smallest group - SOG were identified. From all patients eligible for SOG, the sample of comparable size, and the optimal age and gender matching was selected. Finally, similar procedure as for SOG was done for selecting the patients for OG.

### Continuous positive airway pressure (CPAP) therapy and polysomnographic monitoring

All subjects received the diagnostic polysomnography (psg) (baseline), followed by two polysomnographies with manual CPAP titration and the control psg (follow up) three months thereafter. During control psg the CPAP pressure was slightly changed in some subjects to compensate the residual respiratory events or to improve the tolerance of the therapy. At follow up the mean CPAP use was also evaluated by reading the CPAP-counter. The sleepiness level was assessed at baseline by Epworth sleepiness scale (ESS) (17). The sleep was recorded with a 16-channel polygraph (Jager-SL 1000 P Polysomnograph, Jager GmbH, Wurzburg, Germany). For electroencephalogram at least four electrodes were mounted (C3, C4, O1, O2). Electrooculogram and the mentalis EMG were obtained according to standard protocols (18). The respiration was monitored with nasal prongs, with inductance bands, placed around thorax and abdomen and with finger oximeter. The motor leg activity was recorded with tibialis anterior EMG from surface electrodes. All recordings were done in sound attenuated rooms with comfortable temperature and light control. The respiratory events were scored according to AASM criteria (15). The sleep stages were scored using standard criteria (18). The sleep quality was assessed using the following parameters: sleep efficiency (SE), defined as the ratio of the time spent asleep to the time in bed, and REM%, N1%, N2%, N3%, defined as the ratio of the time spent in a given sleep stage to time in bed.

### Data analysis

The assessment of the influence of obesity on sleep was made by comparing the polysomnographic parameters between all three groups in analogous recorded nights (intergroup differences) as well as by comparing the polysomnographic

parameters between baseline and 2<sup>nd</sup> CPAP, between baseline and follow up, and between 2<sup>nd</sup> CPAP and follow up, within each group (interrecording differences). The interrecording differences which reached the statistical significance were then compared with significant interrecording differences of other groups, from the analogous nights.

For intergroup comparison the Mann-Whitney U test was used. The interrecording comparisons were analyzed with the Wilcoxon test for related samples. Considering that the analysis was done between three groups or between three recordings, what increased the number of testing, the Bonferroni correction was applied to reduce the probability of Type I error. The commonly used significance level  $\alpha=0.05$  was therefore divided by the number of between group or between recording comparisons, *i.e.* by 3. Consequently, we considered the differences statistically significant if the respective *p*-value was below  $\alpha^*=0.016$ . For clarity and ease of reading, all *P* values figuring in text are the results of the basic comparative statistics (U or Wilcoxon) multiplied by three. In this nomenclature  $p<0.05$  refers to  $\alpha^*<0.016$ .

Probability of type I error resulting from intragroup testing of multiple parameters was further assessed by controlling the false discovery rate (FDR) (19). This assessment was favorable against additional Bonferroni correction as the analysis concerned various aspects (various polysomnographic parameters) of one effect (sleep quality) and the overall conclusion could not be erroneous if a small fraction of the null hypotheses were falsely rejected (20). The FDR was estimated following the approach of Storey *et al.* (19) according to the equation:

$$\text{FDR}=2W(0.5)\alpha/R(\alpha) (1-(1-\alpha)^m)$$

where *m* is the number of hypotheses tested, *W*(0.5) is the number of *p*-values bigger than 0.5 and *R*( $\alpha$ ) is the number of *p*-values smaller than  $\alpha$  (0.05).

The statistical analysis was made with the SPSS statistical software (version 15.0, SPSS, Chicago, IL).

## RESULTS

The FDR for all tests performed on the polysomnographic parameters was at the level of 0.0725.

### Patients selection

At the time of the data collection, there were 3385 patients in the archive diagnosed with OSA (ICD 10-G47.3). We identified 18 patients (5 women, mean age  $55.2\pm 9.7$  years) meeting inclusion criteria for NG. After selecting the patients meeting inclusion criteria for SOG and matching them for age and gender with NG, the SOG contained 17 patients (5 women, mean age  $55.5\pm 9.4$  years). Finally 18 patients (5 women, mean age  $55.6\pm 9.5$  years) were assigned to OG.

### Clinical data

The mean ESS scores before therapy and the CPAP compliance were not different across the groups. We found no patients with minimal CPAP usage (3 h/night) in NG, one in OG (which is 6% of the patients in OG) and another one in SOG (6% of the patients in SOG). The SOG showed higher CPAP pressure than the NG. The clinical data are summarized in *Table 1*.

### Respiratory parameters

**AHI:** at baseline the OG and the SOG showed higher AHI than the NG (*Table 2*). The significant decrease of AHI was seen

Table 1. Clinical data. ESS - Epworth sleepiness scale. CPAP pressure was higher in severely obese than in non-obese ( $p < 0.01$ ). No other differences between groups were found regarding clinical data.

	NOG	OG	SOG
<b>BMI (kg/m<sup>2</sup>)</b>	23.5 ± 0.9	33.6 ± 2.9	44.0 ± 3.3
<b>ESS</b>	8.9 ± 3.7	9.7 ± 4.6	10.4 ± 4.8
<b>CPAP press (mbar)</b>	7.0 ± 1.2	8.7 ± 1.6	9.9 ± 1.9
<b>CPAP compl. (h/night)</b>	6.1 ± 1.3	6.4 ± 1.1	6.1 ± 1.4

Table 2. Mean values respiratory and sleep profile parameters with differences between groups. AHI – apnea hypopnea index; Min SaO<sub>2</sub> – minimal oxygen saturation during time in bed (TIB); SE – sleep efficiency, N1, N2, N3; REM – percentage of particular sleep stage in TIB. Arrows point the differences between nonobese and severely obese.

BASELINE	NG		OG		SOG
AHI	29.5 ± 18.7	$p=0.01$	66.9 ± 21.6	$p=0.06$	82.3 ± 23.6
Min SaO <sub>2</sub> (%)	83.7 ± 6.6	$p=0.01$	74.4 ± 10.2	$p=0.29$	69.8 ± 8.9
SE (%)	77.9 ± 11.2	$p=1$	77.7 ± 11.8	$p=0.46$	71.0 ± 15.2
N1 (%)	19.2 ± 9.5	$p=0.03$	29.7 ± 13.3	$p=1$	33.2 ± 16.4
N2 (%)	35.5 ± 8.9	$p=0.51$	30.7 ± 11.9	$p=1$	26.5 ± 10.9
N3 (%)	14.9 ± 9.1	$p=1$	12.5 ± 10.6	$p=0.66$	9.0 ± 10.8
REM (%)	8.3 ± 4.2	$p=0.25$	5.8 ± 4.3	$p=1$	4.7 ± 5.2
<b>2nd CPAP</b>					
	NG		OG		SOG
AHI	0.8 ± 1.7	$p=0.61$	1.5 ± 2.1	$p=0.59$	2.0 ± 3.1
Min SaO <sub>2</sub> (%)	91.6 ± 2.6	$p=0.01$	87.9 ± 2.4	$p=0.33$	86.0 ± 3.7
SE (%)	81.1 ± 9.2	$p=0.80$	84.4 ± 9.2	$p=1$	83.8 ± 10.5
N1 (%)	13.3 ± 6.7	$p=0.43$	11.5 ± 7.7	$p=0.43$	7.8 ± 3.8
N2 (%)	31.3 ± 9.5	$p=1$	28.6 ± 8.1	$p=0.38$	24.3 ± 7.9
N3 (%)	25.5 ± 10.3	$p=1$	28.1 ± 10.6	$p=1$	31.8 ± 11.0
REM (%)	11.8 ± 4.0	$p=0.14$	15.8 ± 7.0	$p=0.11$	21.6 ± 7.0
<b>FOLLOW UP</b>					
	NG		OG		SOG
AHI	0.7 ± 1.0	$p=0.88$	1.3 ± 1.9	$p=1$	1.3 ± 2.4
Min SaO <sub>2</sub> (%)	91.7 ± 2.3	$p=0.01$	88.6 ± 2.9	$p=1$	89.3 ± 2.9
SE (%)	80.8 ± 11.7	$p=1$	82.9 ± 14.3	$p=1$	81.1 ± 14.5
N1 (%)	12.4 ± 5.3	$p=0.38$	10.0 ± 5.2	$p=1$	9.5 ± 5.0
N2 (%)	34.2 ± 8.4	$p=1$	32.4 ± 9.3	$p=1$	33.6 ± 8.8
N3 (%)	24.3 ± 7.5	$p=1$	25.4 ± 8.6	$p=1$	22.8 ± 8.5
R (%)	12.6 ± 6.3	$p=0.76$	15.0 ± 7.3	$p=1$	15.2 ± 6.3

in all three groups from baseline to 2<sup>nd</sup> CPAP night and it was more pronounced in OG and SOG than in NG (Table 3). In consequence, no differences in AHI were seen at 2<sup>nd</sup> CPAP between groups (Table 2). The interrecording analysis between

baseline and follow up showed significant decrease of AHI in all groups, which was more pronounced in OG and SOG than in NG (Table 5).

**Min SaO<sub>2</sub>:** in accordance with AHI the min SaO<sub>2</sub> was at baseline lower in OG and SOG than in NG (Table 2). From baseline to 2<sup>nd</sup> CPAP night the overall increase of min SaO<sub>2</sub> was significantly more pronounced in SOG than in NG (Table 3). From 2<sup>nd</sup> CPAP to follow up a significant increase in min SaO<sub>2</sub> was seen only in SOG (Table 4). The comparison of baseline with follow up revealed an increase of min SaO<sub>2</sub> in all three groups. This increase was less pronounced in NG than in two other groups (Table 5).

#### Sleep profile parameters

**SE:** the SE showed no intergroup differences at any recording (Table 2).

**N1%:** at baseline the N1% was higher in OG and SOG than in NG (Table 2). From baseline to 2<sup>nd</sup> CPAP a significant decrease of N1% was observed in all groups. This decrease was more pronounced in OG and in SOG than in NG (Table 3). As consequence, N1% was significantly higher in NG than in SOG at 2<sup>nd</sup> CPAP (Table 2). No differences in N1% were observed between groups at follow up (Table 2). The analysis of the differences between baseline and the follow up showed a significant decrease of N1% in all groups and this decrease was more pronounced in SOG and in OG than in NG (Table 5).

**N2%:** no intergroup differences were observed in N2% across all nights.

**N3%:** no intergroup differences were seen in N3 across all nights.

**REM%:** at baseline the REM% was higher in NG than in SOG (Table 2). From baseline to 2<sup>nd</sup> CPAP an increase was seen in OG and more pronounced increase in SOG (Table 3). According to these findings, at 2<sup>nd</sup> CPAP the REM% was higher in SOG than in NG (Table 2). From 2<sup>nd</sup> CPAP to follow up only SOG showed significant decrease (Table 4). There was no intergroup differences in REM% at follow up (Table 2).

## DISCUSSION

In this study we investigated the direct (*i.e.* independent of apneas and hypopneas) effect of obesity on sleep quality in OSA patients before and during CPAP. Before CPAP, no differences in SE, N2% and N3% were observed between groups. The differences seen in S1% and REM% were the consequence of the higher AHI and lower min SaO<sub>2</sub> in both obese groups. The start of the CPAP-therapy led to dramatic improvement of sleep quality (measured in the second night under CPAP), which was more pronounced in obese and severely obese patients, with marked, transient decrease of light sleep and increase of REM sleep. After three months of CPAP, the sleep quality was comparable in all three groups, what indicates, obesity does not affect directly the sleep in OSA patients. This finding is not in line with previous data for obese without sleep apnea (6, 7).

Table 3. Interrecording comparisons: baseline – 2<sup>nd</sup> CPAP. The values in table show the mean differences between 2<sup>nd</sup> CPAP and baseline for each parameter in each group with significance level in regular font. The *P* corresponds to comparisons of the interrecording differences between groups. (It was calculated only for interrecording differences which had reached the statistical significance).

	BASELINE TO 2 <sup>nd</sup> CPAP		
	NG	OG	SOG
AHI	-28.6 ±18.4 P=0.01	-65.4 ±21.4 P=0.01	-80.3 ±23.6 P=0.01
	P=0.01		P=0.14
	P=0.01		
min SaO <sub>2</sub>	+7.9 ±5.8 P=0.01	+13.5 ±9.8 P=0.01	+16.2 ±10.3 P=0.01
	P=0.1		P=0.59
	P=0.01		
SE (%)	+3.2 ±11.2 P=0.95	+6.7 ±12.2 P=0.14	+12.8 ±14.7 P=0.01
N1 (%)	-5.8 ±9.3 P=0.04	-18.2 ±13.1 P=0.01	-25.4 ±17.4 P=0.01
	P=0.01		P=0.48
	P=0.01		
N2 (%)	-4.4 ±8.9 P=0.14	-2.2 ±10.3 P=1	-2.3 ±14.7 P=1
N3 (%)	+10.6 ±12.6 P=0.01	+15.6 ±13.1 P=0.01	+22.8 ±15.3 P=0.01
	P=0.51		P=0.29
	P=0.02		
R (%)	+3.5 ±5.5 P=0.08	+10.1 ±6.7 P=0.01	+16.9 ±8.3 P=0.01
	P=0.02		

Table 4. Interrecording comparisons: 2<sup>nd</sup> CPAP – follow up. The values in table show the mean differences between 2<sup>nd</sup> CPAP and baseline for each parameter in each group with significance level in regular font.

	2 <sup>nd</sup> CPAP TO FOLLOW UP		
	NG	OG	SOG
AHI	-0.1 ±1.8 P=1	-0.1 ±2.5 P=1	-0.6 ±1.4 P=0.23
min SaO <sub>2</sub>	+0.2 ±3.4 P=0.99	+0.7 ±3.1 P=1	+3.3 ±3.5 P=0.01
SE (%)	-0.3 ±11.0 P=1	-1.5 ±12.4 P=1	-2.8 ±15.1 P=1
N1 (%)	-0.9 ±7.2 P=1	-1.5 ±8.4 P=1	+1.7 ±5.0 P=0.41
N2 (%)	+3.2 ±11.3 P=1	+3.8 ±8.5 P=0.17	+9.4 ±11.9 P=0.02
N3 (%)	-1.2 ±12.5 P=1	-2.7 ±11.7 P=0.8	-9.0 ±11.4 P=0.03
R (%)	+0.8 ±4.4 P=1	-0.8 ±6.8 P=1	-6.4 ±7.8 P=0.02

Controlling the false discovery

FDR was at the level of 0.0725. This means that about 7% of the statistically significant p-values could occur by chance. This

value is only slightly higher than the significance level commonly used in the inferential statistics. We therefore conclude, the relatively high number of statistical testing could not bias our conclusions significantly.

Table 5. Interrecording comparisons: baseline – follow up. The values in table show the mean differences between 2<sup>nd</sup> CPAP and baseline for each parameter in each group with significance level in regular font. The *P* corresponds to comparisons of the interrecording differences between groups. (It was calculated only for interrecording differences which had reached the statistical significance).

	BASELINE TO FOLLOW UP		
	NG	OG	SOG
AHI	-28.8 ±18.7 P=0.01	-65.6 ±21.6 P=0.01	-80.9 ±23.7 P=0.01
	P=0.01		P=0.07
min SaO <sub>2</sub>	+8.1 ±6.6 P=0.01	+14.2 ±9.8 P=0.01	+19.5 ±9.5 P=0.01
	P=0.13		P=0.25
SE (%)	+2.9 ±11.1 p=0.69	+5.2 ±12.8 p=0.14	+10.0 ±16.5 P=0.89
N1 (%)	-6.7 ±9.5 P=0.02	-19.7 ±11.9 P=0.01	-23.7 ±16.6 P=0.01
	P=0.01		p=1
N2 (%)	-1.3 ±10.5 p=1	+1.6 ±12.8 p=1	+7.1 ±14.4 p=0.19
N3 (%)	+9.4 ±11.6 P=0.02	+12.9 ±13.7 P=0.01	+13.8 ±9.2 P=0.01
	p=1		p=1
R (%)	+4.3 ±7.8 P=0.1	+9.3 ±6.8 P=0.01	+10.5 ±6.1 P=0.01
	p=0.85		p=1

#### Untreated patients

In untreated OSA, the obesity is associated with more severe disturbances of the nocturnal breathing, what is reflected by lower min. SaO<sub>2</sub> and higher AHI in OG and SOG than in the NG. These results confirm the well known correlation between BMI and AHI (21). Disordered nocturnal breathing influences negatively the sleep quality by prolonging the light sleep (N1), which was higher in both obese groups than in the NG and by reducing the REM% which was lower in SOG than in NG. SE, N2% and N3% were comparable among all three groups and were therefore influenced neither directly nor indirectly by obesity.

#### Acute effect of continuous positive airway pressure (CPAP)

In the 2<sup>nd</sup> night under CPAP the respiratory parameters showed improvement in all groups, but this improvement was more pronounced in both obese groups than in NG. The abolition of respiratory events was associated with improvement in sleep quality expressed primarily by decrease of N1 and increase of N3 in all groups as well as increase of REM% in both obese groups. The intergroup differences between NG and SOG in N1% and REM% had at 2<sup>nd</sup> CPAP inverse direction when compared to baseline *i.e.* N1% was higher in NG and REM% was higher in SOG. Taken into account that the intergroup differences in N1% and REM% were not observed later at follow up, we assume there was a transient rebound of REM sleep and also of sleep stages other than N1, resulting in N1% decrease directly after CPAP start in SOG. Further evidence for this transient effect was the significant decrease of REM sleep and N3 from 2<sup>nd</sup> CPAP to follow up in the SOG. Interestingly, this decrease was associated with an increase of N2, while N1 remained unchanged from 2<sup>nd</sup> CPAP to follow up. Thus, the sleep time gained from N1 to N3

and REM during 2<sup>nd</sup> CPAP was then transferred to N2 and not back to N1 during follow up in the SOG.

The rebound phenomenon was previously described in OSA patients by Fietze *et al.* (1) but in this study it was observed only in severely obese patients with severe OSA before treatment. The reason for this difference is probably the more profound deprivation of REM and N3 stages prior to CPAP in SOG.

#### Long-term effect of continuous positive airway pressure (CPAP)

After three months of CPAP no differences in sleep stages and SE were found between groups. This finding shows the obesity does not affect the sleep in absence of apneas and hypopneas and therefore is discordant to results of Vgontzas *et al.* and Resta *et al.* (6, 7). We propose several reasons accounting for this. The first one may be the snoring present in 46.7% of obese subjects examined by Resta *et al.* and only in 8.1% of the non-obese controls. Our archive data did not include detailed snoring prevalence (it was not reported by Vgontzas as well) but it is to assume that no significant snoring was present under the CPAP pressure sufficient to abolish apneas and hypopneas. Snoring is known to decrease SE and to increase arousals (22). It is therefore possible that the abolition of snoring by CPAP in all our groups contributed to the similar sleep efficiency among them.

Another explanation for the discordance between results of Resta and Vgontzas and those presented herein can be the sleep disturbing effect of the CPAP therapy. The frequent nocturnal awakenings, facial pain, upper airway dryness, allergic rhinitis, and skin lesions (13, 23) are examples of the typical patients' complaints which can lead to the decreased sleep quality and mask the effect of obesity. Third factor can be the relative small sample size in our study. The cohorts of Resta *et al.* and of Vgontzas *et al.* outnumbered ours approximately three times and

had therefore respectively greater sensitivity for the potential effect of obesity on sleep quality.

*Decreased Min SaO<sub>2</sub> under continuous positive airway pressure (CPAP) in obese and severely obese patients*

Both obese groups showed lower min SaO<sub>2</sub> in 2nd CPAP and in follow up nights than NG. Similar findings have been observed previously by Baenrjee *et al.* (24). In that study of the obese OSA patients with persistent hypoxemia under CPAP, the nocturnal capnometry revealed coexistent obesity-related hypoventilation syndrome. This syndrome is closely associated with fatigue and may indicate coexistent disorder like COPD or idiopathic pulmonary fibrosis (25). Further, nocturnal hypoxemia may require an oxygen supply as the sole therapy or as an adjuvant to CPAP (26). Our finding underlines therefore, the need of regular screening of patients under CPAP which includes also the oximetry and if possible capnometry.

*Study limitations*

The retrospective character of the study implies the lack of some data which were beyond the clinical routine, such as monitoring of the daytime sleepiness across the therapy. The only available measurement is the ESS before CPAP. This precludes the assessment if obesity can be the cause of the previously described persistent daytime sleepiness under CPAP. With our results we can only assume that the potential effect of obesity on the sleepiness level in patients under CPAP is not mediated through disordered nocturnal sleep. Another shortcoming is the lack of the scoring of nocturnal arousals. The arousal index is considered to be strongly associated with the restorative function and with overall quality of the sleep. In the study of Resta *et al.* the arousal index was however similar between OG and NG without OSA, while other sleep parameters differed significantly (7). It is therefore possible that our groups have comparable arousals at least under CPAP therapy.

In summary the results confirm the association between obesity and OSA severity in untreated patients. A rebound of REM and deep sleep was observed as the acute effect of CPAP. While it was known in the previous study (1), our data confine it to severely obese patients. Contrary to our expectations, during long term CPAP therapy, the sleep profile is similar in obese and nonobese OSA patients. Thus we conclude, in OSA patients obesity has no direct effect on sleep quality. Finally, the decreased min SaO<sub>2</sub> despite abolished apneas and hypopneas under CPAP, may reflect the coexistent hypoventilation syndrome in some of the obese patients.

Conflict of interests: None declared.

REFERENCES

- Fietze I, Quispe-Bravo S, Hansch T, Rottig J, Baumann G, Witt C. Arousals and sleep stages in patients with obstructive sleep apnea syndrome: Changes under nCPAP treatment. *J Sleep Res* 1997; 6: 128-133.
- Glebocka A, Kossowska A, Bednarek M. Obstructive sleep apnea and the quality of life. *J Physiol Pharmacol* 2007; 58(Suppl. 5): 685-690.
- Wierzbicka A, Rola R, Wichniak A, Richter P, Ryglewicz D, Jernajczyk W. The incidence of sleep apnea in patients with stroke or transient ischemic attack. *J Physiol Pharmacol* 2006; 57(Suppl 4): 385-390.
- Sasanabe R, Banno K, Otake K, *et al.* Metabolic syndrome in Japanese patients with obstructive sleep apnea syndrome. *Hypertens Res* 2006; 29: 315-322.
- Magee CA, Iverson DC, Caputi P. Sleep duration and obesity in middle-aged Australian adults. *Obesity (Silver Spring)* 2010; 18: 420-421.
- Vgontzas AN, Bixler EO, Tan TL, Kantner D, Martin LF, Kales A. Obesity without sleep apnea is associated with daytime sleepiness. *Arch Intern Med* 1998; 158: 1333-1337.
- Resta O, Foschino Barbaro MP, Bonfitto P, *et al.* Low sleep quality and daytime sleepiness in obese patients without obstructive sleep apnoea syndrome. *J Intern Med* 2003; 253: 536-543.
- Birketvedt GS, Florholmen J, Sundsfjord J, *et al.* Behavioral and neuroendocrine characteristics of the night-eating syndrome. *JAMA* 1999; 282: 657-663.
- Heptulla R, Smitten A, Teague B, Tamborlane WV, Ma YZ, Caprio S. Temporal patterns of circulating leptin levels in lean and obese adolescents: relationships to insulin, growth hormone, and free fatty acids rhythmicity. *J Clin Endocrinol Metab* 2001; 86: 90-96.
- Chorostowska-Wynimko J, Plywaczewski R, Jonczak L, *et al.* Leptin measurement in urine is a reliable method of monitoring its secretion in patients with obstructive sleep apnea syndrome. *J Physiol Pharmacol* 2007; 58(Suppl. 5): 105-115.
- Dixon JB, Dixon ME, O'Brien PE. Depression in association with severe obesity. *Arch Intern Med* 2003; 163: 2058-2065.
- Antczak J, Horn B, Richter A, Jernajczyk W, Bodenschatz R, W Schmidt EW. The influence of obesity on sleep quality in male sleep apnea patients before and during therapy. *J Physiol Pharmacol* 2008; 59(Suppl 6): 123-134.
- Guilleminault C, Philip P. Tiredness and somnolence despite initial treatment of obstructive sleep apnea syndrome (what to do when an OSAS patient stays hypersomnolent despite treatment). *Sleep* 1996; 19(Suppl. 9): S117-S122.
- Antczak J, Popp R, Hajak G, Zulley J, Marienhagen J, Geisler P. Positron emission tomography findings in obstructive sleep apnea patients with residual sleepiness treated with continuous positive airway pressure. *J Physiol Pharmacol* 2007; 58(Suppl. 5): 25-35.
- American Academy of Sleep Medicine. 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.
- National Institute of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: executive summary. Expert Panel on the Identification, Evaluation, and Treatment of Overweight in Adults. *Am J Clin Nutr* 1998; 68: 899-917.
- Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991; 14: 540-545.
- Silber MH, Ancoli-Israel S, Bonnet MH, *et al.* The visual scoring of sleep in adults. *J Clin Sleep Med* 2007; 15: 121-131.
- Storey JD. A direct approach to false discovery rates. *J R Stat Soc B Stat Methodol* 2002; 64: 479-498.
- Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc B Stat Methodol* 1995; 57: 289-300.
- Quera-Salva MA, Guilleminault C, Partinen M, Jamieson A. Determinants of respiratory disturbance and oxygen saturation drop indices in obstructive sleep apnoea syndrome. *Eur Respir J* 1988; 1: 626-631.
- Guilleminault C, Stoohs R, Duncan S, Snoring I. Daytime sleepiness in regular heavy snorers. *Chest* 1991; 99: 40-48.
- Hoffstein V, Viner S, Mateika S, Conway J. Treatment of obstructive sleep apnea with nasal continuous positive airway pressure. Patient compliance, perception of benefits, and side effects. *Am Rev Respir Dis* 1992; 145: 841-845.

24. Banerjee D, Yee BJ, Piper AJ, Zwillich CW, Grunstein RR. Obesity hypoventilation syndrome: hypoxemia during continuous positive airway pressure. *Chest* 2007; 131: 1678-1684.
25. Rasche K, Orth M. Sleep and breathing in idiopathic pulmonary fibrosis. *J Physiol Pharmacol* 2009; 60 (Suppl. 5): 13-14.
26. Frohnhofen H, Heuer HC, Kanzia A, Firat A. Influence of type of treatment for sleep apnea on activities of daily living in a sample of elderly patients with severe sleep apnea. *J Physiol Pharmacol* 2009; 60(Suppl. 5): 51-55.

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