# INVESTIGACIÓN ORIGINAL

## PREVALENCE AND FACTORS AFFECTING REM AND SLOW WAVE SLEEP REBOUND ON CPAP TITRATION STUDY IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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**Summary**

**Background.** In patients with obstructive sleep apnea syndrome (OSAS) treatment with CPAP results in an increase of REM sleep and slow wave sleep, but there is limited information about the prevalence of REM rebound in patients with OSAS and possible factors related to the rebound.

**Objective.** REM rebound (RR) and slow wave sleep rebound (SWSR) has been described as a frequent phenomenon that occurs during CPAP titration, but the quantity that qualify for RR has not been mentioned in literature. The objective of our study was to determine the prevalence of REM rebound and slow wave sleep rebound in our sleep disorders center, to attempt to define RR and look for factors that may affect RR and SWSR on the first night of CPAP titration.

**Materials and methods.** We included patients who had both baseline polysomnogram (bPSG) and CPAP polysomnogram (cPSG) studies done in the same laboratory. We included 179 patients>18 years with Apnea hypopnea index (AHI)>10/hr on the baseline study, with an adequate CPAP titration study. We compared the percentages of REM sleep and slow wave sleep during bPSG and cPSG. We analyzed the frequency of presentation and looked for the factors affecting RR and SWSR.

**Results.** 179 patients were enrolled (M/F:118/61), with a mean age of 48.6±4 for men, and 51.6±12.9 for women. The mean interval between the bPSG and cPSG was 45 days. The mean REM percentage during the bPSG was 15.55 percent and during cPSG study it was 21.57 percent. We took 6 percent as our differential point as the results became statistically significant at this point (p:0001). We therefore present our data by dividing our patients population with RR<6% and RR>6%. The mean SWS percentage during the bPSG was 8.11±9.68 and during the cPSG was 13.17±10, with a p:0.35 which is not statistically significant. The multiple regression model showed that the variables that contribute more to the REM change are: REM sleep during bPSG (-0.56), bAHI (0.24) and the body mass index (0.081).

**Conclusions.** We suggest that an increase greater than 6% in REM sleep should be considered REM rebound, since 6.15 percent was the statistically significant difference between bPSG REM sleep and cPSG. The prevalence of RR in our group was 46 percent and the variables that contribute more to RR are REM sleep during bPSG, AHI at baseline and body mass index.

**Key words:** sleep deprivation, prevalence, titrimetry (titration), sleep apnea, obstructive.

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**Resumen**

**Antecedentes.** En pacientes con síndrome de apnea obstructiva del sueño (SAOS) el tratamiento con CPAP produce un incremento en el sueño REM y el sueño profundo, pero no hay suficiente información acerca de la prevalencia del rebote de sueño REM en pacientes con SAOS y los posibles factores relacionados con este fenómeno.

**Objetivo.** El rebote de sueño REM (RR) y del sueño de ondas lentas (RSOL) ha sido descrito como un fenómeno de frecuente presentación que ocurre durante la titulación de la presión del CPAP, pero la cantidad en el incremento del estado de sueño que lo califique como rebote no ha sido mencionado en la literatura. El objetivo del estudio fue determinar la prevalencia de RR y RSOL en nuestro centro de sueño e intentar definir RR y buscar los factores que puedan afectar el RR y el RSOL en la primera noche de titulación de CPAP.

**Material y métodos.** Se incluyeron pacientes que tenían polisomnograma de base (bPSG) y PSG con CPAP (cPAG) realizados en un laboratorio del sueño. Se incluyeron 179 pacientes mayores de 18 años con índice de apneas-hipopneas (IAH) mayor de 10/hora en el estudio de base, con titulación de CPAP adecuada. Se comparó los porcentajes de sueño REM y sueño profundo durante el bPSSG y cPSG. Se analizó la frecuencia de presentación y los factores que afectan el RR y el RSOL.

**Resultados.** Se incluyeron 179 pacientes (M/F 118/61), con edad promedio de 48.6 años ±12.9 para hombres y 51.6±12.9 para mujeres. El intervalo entre el bPSG y el cPSG fue 45 días promedio. El promedio de sueño REM durante el bPSG fue 15.55 por ciento y durante el bPSG 21.57 por ciento. Se tomó seis por ciento como nuestro punto diferencial que resultó estadísticamente significativo (p:0001). Se dividió la población de pacientes en aquellos con RR meno del seis por ciento y RR mayor del seis por ciento. El porcentaje promedio del SOL durante el bPSG fue 8.11±9.68 y durante el cPSG 13.17±10 con una p: 0.35 que no es estadísticamente significativo. El modelo de regresión múltiple mostró que las variables que contribuyeron más al RR fueron: la cantidad de sueño REM durante el bPSG (-0.56), bIAH (0.24) y el índice de masa corporal (0.81).

**Conclusiones.** Se sugiere que un incremento mayor al seis por ciento en sueño REM se debería considerar rebote del sueño REM, ya que 6.15 por ciento fue una diferencia estadísticamente significativa entre el REM del bPSG y del cPSG. La prevalencia del RR en nuestro grupo fue del 46 por ciento y las variables que contribuyen más al RR son la cantidad del sueño REM durante el bPSG, IAH en el bPSG y el índice de masa corporal.

**Palabras clave:** privación de sueño, prevalencia, sueño, titremetría, apnea del sueño obstructivo.

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## Introduccion

In patients with obstructive sleep apnea syndrome (OSAS), Rapid Eye Movement (REM) sleep is usually fragmented, often because the apneas occur with particular frequency during this sleep stage. Some OSAS patients may remain REM sleep deprived for many years. With successful treatment of OSAS with CPAP, patients can again have extended periods of REM sleep. This accumulated REM deprivation can lead to increase in REM sleep time and REM density on the night of the CPAP titration (REM rebound) (1,2). RR is well known in sleep literature. The amount of RR varies considerably and may be related to many factors. Different authors have mentioned a substantial RR on the CPAP trial night in comparison to the baseline study (1-4) but did not address the prevalence and factors affecting REM rebound.

The amount of RR in these patients was addressed as substantial but was not defined (1). Weitzman and colleaguess., showed an increase in slow wave sleep (SWS) but not in REM sleep after tracheostomy (5) and others have shown rebound in both REM sleep and SWS (3,5). Verma et al in 2001 made similar attempts to see the affect of RR and SWSR on subjective quality of sleep (6). ASDA refer to REM rebound as a significant increase in REM sleep on CPAP titration (7).

Parino et al in 2000 described the sleep reactivity during CPAP treatment and emphasized increased CAP rate, CAP time and number of CAP cycles (8). In all these studies, RR and SWSR was noted and referred to as statistically significant. To our knowledge no attempt has so far been made to define the amount of REM sleep to qualify as REM rebound. The objective of our study was to determine the prevalence of REM rebound and slow wave sleep rebound in our sleep disorders center, to attempt to define RR and look for factors that may affect RR and SWSR on the first night of CPAP titration.

## Materials and methods

### Subjects

We picked up a specific date and included patients with an adequate CPAP titration study (cPSG). We defined adequate titration if the corrected AHI on CPAP titration was smaller that 10/hr and the sleep efficiency was greater tha 50 percent. We then collected baseline polysomnogram (bPSG) data of these patients. We included 204 sequential patients with adequate titration study coming to the sleep laboratory at JFK medical center for over a period of 12 months. We included patients who had both baseline polysomnogram (bPSG) and CPAP polysomnogram (cPSG) studies done in the same laboratory. We included 179 patients greater that 18 years with Apnea hypopnea index (AHI) greater that 10/hr on the baseline study with an adequate CPAP titration study. We excluded 23 patients with sleep efficiency smaller that 50 percent during the bPSG, one patient with mental retardation and one patient with tracheotomy. The factors that we looked for were age, sex, BMI, baseline AHI, REM sleep on bPSG and CPAP pressure and minimum desaturation.

### Data Collection

We recorded 4 channels of EEG using referential leads and international nomenclature (C3–A2, O1-A2, C4-A1, O2-A1). Right and left electroculograms (ROC and LOC) and submental electromyogram (chin EMG) were recorded using electrodes. The airflow was monitored by a nasal pressure tansducer and the electrocardiogram (EKG) was monitored by a single chest lead. The respiratory effort was monitored by the abdominal and the thoracic belts, and the limb movements were monitored by EMG leads on the tibialis anterior and gastroctnemius muscles on both legs. The oxygen saturation was monitored by finger pulse oximetery. The CPAP titration was done by a certified technologist. The pressure was increased by 2 cm H2O to correct for snoring, apneas, hypopneas, arousals and desaturations. The patients were titrated in supine position and REM sleep to correct for the above-mentioned elements. Sleep stages and respiratory events were defined by the standard criteria (7). Apnea was defined as a complete cessation of airflow for at least 10 seconds, hypopnea was defined as a reduction in airflow that was at least 10 seconds in duration and was associated with an electroencephalographic arousal or a 3 percent or more drop in the oxygen saturation (8).

We collected the following data from the bPSG and cPSG: age, gender, Body mass Index(BMI),

**Table 1.** *Patients demographic and polysomnographic charecteristics*

| | **RR<6%** | | **RR>6%** | |
|---|---|---|---|---|
| | 97/179 (54%) | | 82/179 (46%) | |
| | **M** | **F** | **M** | **F** |
| | 59 (61%) | 38 (39%) | 59 (72%) | 23 (28%) |
| Age (yrs) | 52±13.5 | 51±13 | 45.2±13.8 | 51.2±12.9 |
| BMI (kg/m2) | 33.0±7.9 | 38.4±7.9 | 34.3±7.6 | 40.4±8.6 |
| AHI /hr | 41.9±25.7 | 32.8±24.8 | 58.1±26.9 | 38±25.6 |
| REM AHI/hr | 47.7±20.7 | 49.6±23.5 | 52.9±28.9 | 57.2±23.7 |
| REM % TST | 19.3±5.8 | 18.6±7.4 | 11.7±7.0 | 15.3±6.4 |
| MEAN SAO2% | 92.8±3.2 | 93.7±3.2 | 92.2±3.2 | 93.2±2.6 |

***BMI:*** *Body Mass Index,* ***AHI:*** *Apnea Hypopnea Index,* ***REM AHI:*** *AHI during REM sleep,* ***TST:*** *Total Sleep Time.*

Sleep efficiency(SE), Arousal Index (AI), Wake after sleep onset (WASO), stage transitions (ST), awakenings, sleep latency (SL), REM latency, REM cycles in first half of night and second half of night, baseline AHI, REM AHI (AHI when the patient was in stage REM), NREM AHI (AHI when the patient was in stage NREM), percentages of sleep stages 1, 2, slow wave sleep and REM sleep, mean oxygen saturation, mean oxygen saturation during desaturation, minimum oxygen saturation, medical conditions and medications. We took the difference of percentage of REM sleep between the cPSG and bPSG and called it REM rebound (RR). We took the difference of percentage of slow wave sleep between the cPSG and bPSG and called it slow wave rebound (SWSR). We also collected questionnaire data to analyze the subjective improvement on the cPSG. This questionnaire is a validated instrument used in our sleep lab for the assessment of sleep quality on the night of the bPSG and cPSG. We divided medications into four groups: benzodiazepines, antidepressants, antihypertensive and others.

#### Statistical Analysis

We applied a paired t-Student test to compare the mean percentage of REM sleep between the bPSG and cPSG, and a t-test to compare the REM rebound by gender. A Kruskal-Wallis test was applied to determine the significance in the mean SWS between bPSG and cPSG. We did a correlation matrix with a Pearson's test between REM rebound and gender, age, CPAP pressure, body mass index, AHI of the bPSG, mean SaO2 of bPSG. A multiple regression model was applied to measure the weight of each variable to explain the variation in REM sleep percentage. To choose the best model that explains the REM change with CPAP we applied a backwards-stepwise regression.

## Results

179 patients were enrolled (M/F:118/61), with a mean age of 48.6±4 for men, and 51.6±12.9 for women. The mean interval between the bPSG and cPSG was 45 days. The mean REM percentage during the bPSG was 15.55 percent and during cPSG study it was 21.57 percent (Figure 1). We took 6 percent as our differential point as the results became statistically significant at this point (p:0.0001). The major result of this study is that 46 percent of our patient population had greater that 6 percent of RR on the CPAP titration study. We present our data by dividing our patients population with RR smaller that 6

**Table 2.** *Multiple regression analysis that correlates REM rebound to BMI, bREM, bREM RDI, bRDI, bMean SaO2*

| rr | Coef. | Std. | Err. | t | P>\|t\| | [95% Conf. Interval] |
|---|---|---|---|---|---|---|
| BMI | .1442353 | .0818212 | 1.76 | 0.080 | -.0173161 | .3057868 |
| bREM | -.7510754 | .0857529 | -8.76 | 0.000 | -.9203898 | -.5817609 |
| bREM-RDI | .0023222 | .0355589 | 0.07 | 0.948 | -.0678869 | .0725314 |
| bRDI | .0927521 | .0327439 | 2.83 | 0.005 | .028101 | .1574031 |
| bMean SaO2 | .1101954 | .2322513 | 0.47 | 0.636 | -.3483721 | .5687629 |
| _cons | -1.996744 | 23.25813 | -0.09 | 0.932 | -47.91866 | 43.92517 |

***BMI:*** *Body Mass* Index, **bREM:** baseline REM, **bREM-RDI:** RDI during baseline REM sleep, **bRDI:** global baseline RDI (NREM and REM), **bMean SaO2:** baseline mean SaO2

percent and RR greater that 6 percent (Table 1). There was no significant difference by gender in REM rebound (p: 0.47). The correlation matrix of REM rebound showed a significant correlation with body mass index (p 0.080), bPSG stage REM (p 0.0001) and bPSG AHI (p 0.005). The multiple regression model showed that the variables that contribute more to the REM rebound, according to the regression coefficient are: REM sleep during bPSG, bAHI and the body mass index (Table 2, Figure 2). These findings were corroborated with the stepwise regression analysis. Medications did not show a correlation with REM rebound.

The mean SWS percentage during the bPSG was 8.11±9.68 and during the cPSG was 13.17 ± 10. We observed a 5 percent change in SWS on the cPSG, with a p:0.35 which did not reach statistical significance (Figure 3). We tried to correlate our data with the questionnaire information but did not find any correlation.

## Discussion

The effective use of CPAP is accompanied not only by a significant reduction in the AHI, but also in the arousal index, oxygen saturation and an increase of REM sleep (REM rebound) and SWS. REM rebound has been described repeatedly in the patients of OSAS since the initial days of use of CPAP (1,2). It has also been noted that not all patients respond to CPAP similarly despite adequate titration i.e. the amount of REM sleep increase on the night of CPAP titration has been seen to be variable. Verma et al looked at the subjective quality of sleep following the first night of treatment with CPAP and attribute the improvement in sleep to the amount of REM rebound (6) and recent studies looked at the cyclic alternate pattern (CAP) rate variability but in the papers mention above there is no definition for REM rebound and the factors that will affect its occurrence have not been looked into. The objective of our study was to determine the prevalence of REM rebound and slow wave sleep rebound in our sleep disorders center, to attempt to define RR and look for factors that may affect RR and SWSR on the first night of CPAP titration. We selected patients with adequate titration i.e. the AHI was reasonably corrected. We found that in our patient population 46 percent have greater that 6 percent of RR. We suggest REM rebound should be considered as 6.15 percent since this was the statistically significant difference between bPSG REM sleep and cPSG (p:0.0001). Verma et al also found similar result of RR (6). In this population, REM rebound was observed in 45.8 percent of patients (82), 24 women (39.3% from the total of females) and 49 percent men (from the whole group of males). There was no

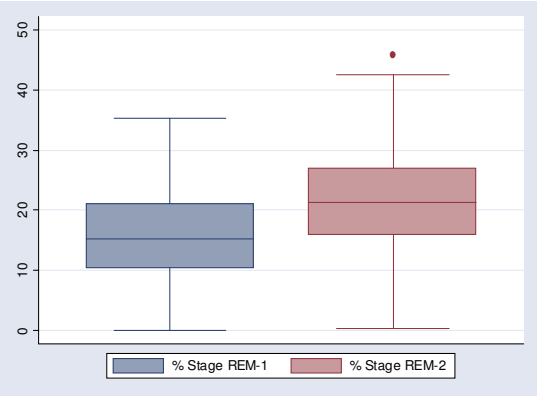


**Figure 1.** *Box plot showing baseline REM (bREM-REM-1) percentage and CPAP REM percentage (REM-2). There is difference that reach statistically significant level*

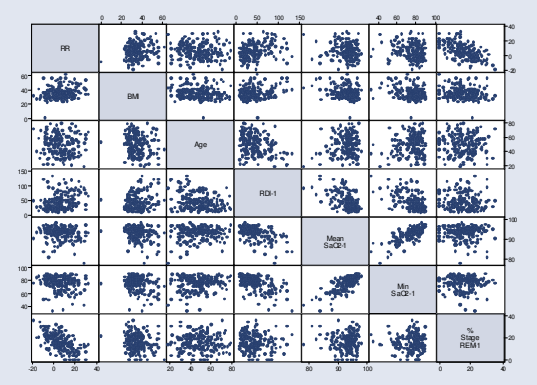


**Figure 2.** *Linear correlation between RR (REM REBOUND) and % of stage REM-bPSG, Min SaO2, Mean SaO2, AHI-bPSG, Age and BMI.*

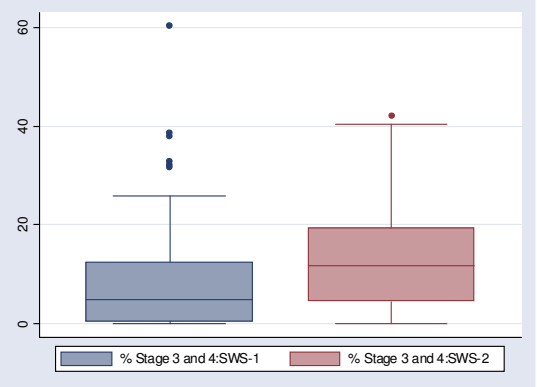


**Figure 3.** *Box plot showing baseline NREM (bNREM) percentage and CPAP NREM percentage (cNREM). There is a difference but it does not reach statistically significante level.*

difference in the mean amount of REM rebound between sex, mean REM rebound 14.48 for men and 15.98 for women. The factors that we looked for were age, sex, BMI, baseline AHI, REM sleep on bPSG and CPAP pressure and minimum desaturation. The factors that contributed more to RR were REM sleep during bPSG (-0.56), bAHI (0.24) and body mass index (0.081). Like Verma et al. in our sample we found a difference in SWS between bPSG and cPSG but did not reach statistical significance. The mean SWS percentage during the bPSG was 8.11±9.68 and during the cPSG was 13.17±10 (p:0.35). Medications did not contribute to RR or SWSR. As this was a retrospective study, we did not have clinical interview post CPAP on these patients but we did have pre and post study sleep questionnaire on these patients. The data from these questionnaires did not correlate with the statistically significant number of RR or SWSR.

There are several weaknesses in our study; firstly it is a retrospective data. There is a selection bias as this was a convenience sample of a sleep lab population. We did try to eliminate the factor of inadequate titration. We selected patients on medications but our statistical analysis did not show any effect of medication on RR. We do not have MSLT data to support the daytime effect of the 6 percent RR that we saw in our patient population. We do not have acclimatization night data.

Further prospective studies need to be done to confirm our observation that more than half the patients coming to a sleep lab for a CPAP titration do not get RR and SWSR and the factors that relate to this phenomenon.

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