The Art of Titration

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Objectives:

- Discuss the physiology of obstructive sleep apnea
- Describe the role and mechanism of action for PAP
- Review the titration guidelines
- Improve the quality of CPAP titrations
Art of PAP titration

David Bradshaw, MD
Overview

- Classification of sleep related breathing disorders
- Pathophysiology of airway obstruction
- Brief History of PAP therapy
- Current AASM titration recommendations
- APAP
- Titration tips
- Advanced therapies
Sleep Related Breathing Disorders ICSD-3

(ICD -9-CM/ICD-10-CM)

- **Obstructive Sleep Apnea**
  - Adult (327.23/G47.33)
  - Pediatric (327.23/G47.33)

- **Central Sleep Apnea Syndromes**
  - Central Sleep Apnea with Cheyne-Stokes Breathing (786.04/R06.3)
  - Central Sleep Apnea Due to a Medical Disorder without Cheyne-Stokes Breathing (327.27/G47.37)
  - Central Sleep Apnea Due to High Altitude Periodic Breathing (327.22/G47.32)
  - Central Sleep Apnea Due to a Medication or Substance (327.29/G47.39)
  - Primary Central Sleep Apnea (327.21/G47.31)
  - Primary Central Sleep Apnea of Infancy (770.81/P28.3)
  - Primary Central Sleep Apnea of Prematurity (770.82/P28.4)
  - Treatment Emergent Central Sleep Apnea (327.29/G47.39)

- **Sleep Related Hypoventilation Disorders**
  - Obesity Hypoventilation Syndrome (278.03/E66.2)
  - Congenital Central Alveolar Hypoventilation Syndrome (327.25/G47.35)
  - Late-Onset Central Hypoventilation with Hypothalamic Dysfunction (327.26/G47.36)
  - Idiopathic Central Alveolar Hypoventilation (327.24/G47.34)
  - Sleep Related Hypoventilation Due to a Medication or Substance (327.26/G47.36)
  - Sleep Related Hypoventilation Due to a Medical Disorder (327.26/G47.36)

- **Sleep Related Hypoxemia Disorder** (326.26/G47.36)

- **Isolated Symptoms and Normal Variants**
  - Snoring (786.09/R06.83)
  - Catathrenia (none)
Sleep Related Breathing Disorders

- Obstructive Sleep Apnea, Adult (327.23/G47.33)
- Obstructive Sleep Apnea, Pediatric (327.23/G47.33)
Pathogenesis of Upper Airway Obstruction During Sleep

**Collapsing Forces**
1. Intraluminal negative pressure
2. Anatomy

**Dilating Forces**
1. Lung volume
2. Pharyngeal dilator muscle activation
Collapsing Forces

- **Intraluminal negative pressure**
  - Generated by diaphragm

- **Anatomy**
  - $P_{\text{crit}}$ (intraluminal pressure at which collapse occurs)
  - $P_{\text{crit}}$ in normal, non-obese is about -5 cm H$_2$O
  - $P_{\text{crit}}$ in OSA patients is greater
  - Obesity, bony restriction, tonsils, adenoids, vascular perfusion, posture, secretions, tissue microstructure
Anatomy

<table>
<thead>
<tr>
<th>Soft tissue</th>
<th>Bony enclosure</th>
<th>Airway size</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>obesity</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Small maxilla &amp; mandible</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

White, AJRCCM 2005
Anatomy

Normal

Patient
Causes of UA Soft Tissue Enlargement

- Edema
  - Repeated airway closure
  - Volume overload states
- Obesity
- Muscle injury
- Gender
- Genetic factors
Static Airway Anatomy in Patients

(Retropalatal)
Figure 2  Possible mechanisms by which “tracheal tug” influences upper airway patency. Reprinted with permission from Van de Graaff.\textsuperscript{17}
**Sleep-Sensitive Neuromodulators**

5HT, Ach, Orexin, Hist, NE

(3-Sleep)

Hypoglossal Motor Nucleus

**Wakefulness Stimulus**

Central Respiratory Pattern Generator

(2-Phasic Respiratory Input)

NTS

Superior Laryngeal (1-Reflex) Nerve

Mechanoreceptors respond to negative pressure

Output to UA and diaphragm – respiratory drive
Sleep-Sensitive Neuramodulators
5HT, Ach, Orexins, Hist, NE

Central Respiratory Pattern Generator
(2-Phasic Respiratory Input)

Hypoglossal Motor Nucleus

NTS

Superior Laryngeal (1-Reflex) Nerve

Genioglossus Muscle

Pharyngeal Airway

White, AJRCCM 2005
Repetitive Apneas

• Anatomically compromised UA, i.e. low $P_{crit}$ (dilator muscles compensate while awake)

• Loss of compensatory neuronal activation at sleep onset leads to narrowing or collapse
  – Poor/inadequate UA dilator muscle response

• Cyclical (repeated) events may occur as the result of multiple compensatory processes
  – High/excessive ventilatory response (loop gain)
  – Low arousal threshold
How do you keep the airway open?
The only treatment we could offer then was a tracheostomy. We had only very, very sleepy patient’s; patients who would come and nearly die each day they drove their car because they were falling asleep within 5 minutes. It was a real catastrophe! We only could offer one treatment, tracheostomy, for severe cases. That was all we had for about 15 years. It saved the life of a number of people, but you can perfectly understand how traumatic it was. There were some children that had this particular problem. The first child to have a tracheostomy in the United States had surgery in 1972 at Stanford. It was difficult to recommend this kind of treatment. There is only one patient in the Bay area that still has a tracheostomy and he is a physician.

A young resident, Colin Sullivan, from Sidney, Australia, came to California with his mentor, David Reed, to a big conference in 1978. In the early 1980s his mentor decided there is something in sleep and breathing and he was going to send his brightest a student to Canada where there was a group during research in sleep and breathing.

Colin Sullivan was sent to Toronto and went back to Sidney with the idea of creating a reverse vacuum cleaner that could possibly open the windpipe of the sleeper. Basically what he did was take an old vacuum cleaner, changed it, reversed it, and tried it on himself. He presented it and tried it on a patient volunteer who is still very much alive. They realized the mask that they had at the time was not fitting very well. They made a mask fitted to the patient. The kept the patient in the hospital for 5 days; the patient decided that was enough. He was leaving the hospital, he had a vacuum cleaner on his face with a mask and he just preferred to take the whole thing home. But he felt so much better, he decided to stay with a vacuum cleaner, which was terrifically improved.
Colin Sullivan presented his results to those in the field, there were not too many of us, about 8 or 10 groups in the world and they decided to create their own vacuum cleaners and that is it! That is the Stanford version of the vacuum cleaner. That is the small model. We then went to South San Francisco where they had a nice blower and we worked with them and built the thing that could really blow a small airplane. There was a little problem because we didn’t want to blow up peoples lungs. We needed a lot of protection so we had a huge filter. It took about 6 months before we had it working properly.

We made a mold for his mask. It took about 3-4 hours to make one mask. We were spending our nights making multiple molds of the face of people to make their masks. It was a craft. Luckily we didn’t have that many patients and we became very good. We decreased our time to make a mask to 90 minutes. Then we had technicians who were able to do it better that we could. We had about 40-45 patients in the Bay area who were using that machine. At the same time there was an entrepreneur named McGinnis in Pennsylvania who thought maybe there was something behind that and it would be a good idea if he would start a business in his garage and start selling the machine that opened the airway and that’s how Respironics got started. I regret that they never offered any stock, otherwise I would probably be rich by now!
The First PAP Titration

REVERSAL OF OBSTRUCTIVE SLEEP APNOEA BY CONTINUOUS POSITIVE AIRWAY PRESSURE APPLIED THROUGH THE NARES

Colin E. Sullivan, Michael Berthon-Jones, Faiq G. Issa, Lorraine Eves
The Lancet, Vol. 317, No. 8225, p862–865
Published in issue: April 18, 1981
“The pivotal moment was a night in June 1980 when we first tested the idea that positive pressure, applied just to the nasal airway, could stop obstructive apnea. Although I had the idea several months previously, at that time we saw only a very few patients, so we had to wait for an appropriate patient to do the experiments. The patient in whom the first test was done had very severe sleep apnea and had come under my care at the Royal Prince Alfred Hospital where I was a physician in the respiratory unit. He was so severe that I recommended a tracheotomy as an urgent procedure. However, he and his family refused surgery, but he was happy to volunteer for the pressure experiment. We put together the breathing circuit in the afternoon, and then used plastic tubes and a rapid setting silicone sealant to provide access to the nasal airway. Within minutes of the full polysomnography (PSG) set up, the patient had gone to sleep and developed repetitive severe sleep apnea. I gradually increased the air pressure in the circuit, and then suddenly the apnea stopped and normal breathing appeared. It was an incredible result. As we watched in amazement, the patient went into REM sleep. I quickly decided to repeat the experiment by dropping the pressure and the apnea recurred. I went through a series of cycles increasing the pressure and so literally “turning off” the apnea, and then dropping the pressure and “turning on” the apnea. There was no uncertainty or ambiguity. The method worked. The effect was so clear and repeatable, the next question to answer was would it work all night?. Could we use it as a treatment? We decided to leave the patient on the pressure for the rest the night. We watched as he continued to sleep for around 7 hours, without any apnea, and with the most extraordinarily intense sleep patterns. The patient’s response the next day was equally exciting. He was awake and alert for the first time in years.”

Colin Sullivan, M.B.B.S. Past, Present and Future of CPAP, NSF 2009
Effect of CPAP on the Upper Airway
Table 1—AASM Classification of Evidence

<table>
<thead>
<tr>
<th>Evidence Levels</th>
<th>Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Randomized well-designed trials with low alpha and beta error*</td>
</tr>
<tr>
<td>II</td>
<td>Randomized trials with high alpha and beta error*</td>
</tr>
<tr>
<td>III</td>
<td>Nonrandomized concurrently controlled studies</td>
</tr>
<tr>
<td>IV</td>
<td>Nonrandomized historically controlled studies</td>
</tr>
<tr>
<td>V</td>
<td>Case series</td>
</tr>
</tbody>
</table>

Table 2—AASM Levels of Recommendations

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>This is a generally accepted patient care strategy that reflects a high degree of clinical certainty. The term standard generally implies the use of level I evidence that directly addresses the clinical issue, or overwhelming level II evidence.</td>
</tr>
<tr>
<td>Guideline</td>
<td>This is a patient care strategy that reflects a moderate degree of clinical certainty. The term guideline implies the use of level II evidence or a consensus of level III evidence.</td>
</tr>
<tr>
<td>Option</td>
<td>Recommendation with less evidence than guideline for which agreement was reached in a standardized consensus process based on available information.</td>
</tr>
</tbody>
</table>

Adapted from Eddy and Iber et al.8

Recommendation

*(standard)*

- All potential PAP titration candidates should receive...
  - PAP education
  - Hands on demonstration
  - Careful mask fitting
  - Acclimatization prior to titration
Recommendation

(consensus)

• Recording the airflow signal generated by the PAP device or estimating airflow by measurement of the pressure difference between the mask and outlet of the machine using a pressure transducer are acceptable for detecting apneas or hypopneas

• Use of a thermistor or thermocouple placed under the PAP mask is not acceptable

Recommendation

(consensus)

• *Respiratory effort-related arousals* may be estimated by flattening of the inspiratory airflow profile associated with an arousal when airflow changes do not meet criteria for apneas or hypopneas.

• *Sawtooth patterns* in the unfiltered airflow or mask pressure tracings or *microphones* applied to the neck are acceptable methods for detecting *snoring*.

Recommendation

(consensus)

• CPAP should be increased until the following obstructive respiratory events are eliminated (no specific order)...
  – Apneas
  – Hypopneas
  – RERAs
  – Snoring
Recommendation

(consensus)

• Starting CPAP pressure 4 cm H₂O in pediatric and adult patients

• Maximum recommended pressure....
   – 15 cm H₂O for < 12 years
   – 20 cm H₂O for ≥ 12 years
   – May switch to BiPAP if obstructive events continue above 15 cm H₂O

CPAP titration algorithm <12 years

Recommended maximum 15 cm H₂O - The patient may be transitioned to BPAP if there are continued breathing events at this pressure**

"Exploration" of pressure

≥ 1 obstructive apnea, or
≥ 1 hypopnea, or
≥ 3 RERAs, or
≥ (1 min of loud or unambiguous snoring)

≥ 1 cm H₂O

≥ 5 min

≥ 30 min without breathing events

Control of breathing events and
≥ 15 min in supine REM sleep

≥ 1 cm H₂O

≥ 10 min

If patient awakens and complains pressure is too high, a lower pressure that the patient reports is comfortable enough to allow return to sleep should be chosen and resume titration.

≥ 1 cm H₂O

Stop if re-emergence of breathing events

CPAP titration algorithm $\geq 12$ years

Recommendation  
(consensus)

• Indications for increasing CPAP
  – At least 1 cm H₂O at intervals of at least 5 min
  – When at least 1 OA is observed in children, or at least 2 OA are observed in adults
  – When at least 1 OH is observed in children, or at least 3 OH are observed in adults
  – When at least 3 RERAs are observed in children, or at least 5 RERAs are observed in adults
  – When at least 1 minute of snoring is observed in children, or at least 3 minutes of snoring is observed in adults
CPAP titration algorithm ≥12 years

Recommendation

*(consensus)*

- “Exploration” of CPAP above the pressure after control of abnormalities in respiratory parameters should not exceed 5 cm H$_2$O
- If the patient awakens and complains of excessive pressure, the pressure should be restarted at a pressure the patient finds comfortable
- “Down” titration may be considered as an option
  - After 30 minutes of control
  - 1 cm H$_2$O no more than every 10 min until events recur

CPAP titration algorithm ≥12 years

Recommendation: Split-Night

*(guideline)*

- Titration algorithm is the same as for a full night
  - Consider increments of 2-2.5 cm H₂O given the shorter CPAP titration duration
  - Insufficient data to make any recommendations for split-night studies in children
Recommendation: BiPAP

(consensus)

• Indications
  – Uncomfortable or intolerant of high CPAP pressure
  – Continued events above 15 cm H2O

• Increase to control apnea, hypopnea, RERA, snoring (no specific order)

• Starting minimum pressure 8/4 (higher for obese or retitration)

• Max IPAP 20 cm H2O for <12, 30 for ≥12

• Min IPAP:EPAP differential 4, max 10
BiPAP titration algorithm <12 years

Recommended maximum IPAP 20 cm

“Exploration” of IPAP

≥ 30 min without breathing events

≥ 1 obstructive apnea, or
≥ 1 hypopnea, or
≥ 3 RERAs, or
≥ (1 min of loud or unambiguous snoring)

Control of breathing events and
≥ 15 min in supine REM sleep

IPAP ≥ 1 cm H₂O

≥ 10 min

If patient awakens and complains pressure is too high, a lower IPAP that the patient reports is comfortable enough to allow return to sleep should be chosen, and resume titration

IPAP ≥ 1 cm H₂O

≥ 5 min

≥ 1 obstructive apnea, or
≥ 1 hypopnea, or
≥ 3 RERAs, or
≥ (1 min of loud or unambiguous snoring)

Stop if re-emergence of breathing events

Minimum*
IPAP 8 / EPAP 4 cm H₂O

≥ 5 min

IPAP and EPAP ≥ 1 cm H₂O for apneas,
IPAP ≥ 1 cm for other events

≥ 5 min

BiPAP titration algorithm ≥12 years

Recommendation: BiPAP

(consensus)

• Indications for increasing BiPAP
  – IPAP and/or EPAP at least 1 cm H2O at intervals of at least 5 min depending on type of respiratory event
  – IPAP and EPAP when at least 1 OA is observed in children, or at least 2 OA are observed in adults
  – IPAP when at least 1 OH is observed in children, or at least 3 OH are observed in adults
  – IPAP when at least 3 RERAs observed in children, or at least 5 RERAs are observed in adults
  – IPAP when at least 1 min snoring in children, or at 3 min snoring observed in adults

BiPAP titration algorithm ≥12 years

Recommendation: BiPAP  
*(consensus)*

- “Exploration” of IPAP above the pressure after control of abnormalities in respiratory parameters should not exceed 5 cm H₂O
- If the patient awakens and complains of excessive pressure, the pressure should be restarted at a pressure the patient finds comfortable
- “Down” titration may be considered as an option
  - After 30 minutes of control
  - 1 cm H₂O no more than every 10 min until events recur
- Decrease IPAP or change to ST mode should be considered if treatment-emergent central apneas occur

BiPAP titration algorithm ≥12 years

Recommendation: Acceptable

(consensus)

• Acceptable = Low RDI (preferably <5), SpO\textsubscript{2} >90%, low leak
  – Optimal
    • Low RDI (<5) for at least 15 min and supine REM
  – Good
    • RDI <10 or by 50% if baseline <15 and supine REM sleep
  – Adequate
    • RDI >10 but by at least 75% from baseline or lack of supine REM sleep

• Unacceptable
Recommendations: Leak and Comfort

*(consensus)*

- **PAP mask refit or readjustment** should be performed whenever any significant unintentional leak is observed
  - Intentional leak is the controlled leak needed to wash out CO$_2$
  - Unintentional leak
    - Mouth leak/oral venting
    - Mask leak
  - Insufficient evidence to define a clinically significant leak
    - Intentional leak vs pressure relationship provided by manufacturer of each interface
  - Pressure waveform modification technologies may improve comfort and adherence (EPR, C-flex)

Pressure Waveform Technologies

**Comfort levels**

EPR provides three comfort settings. Each comfort setting correlates to an exact drop in pressure relief:

- EPR Level 1: Mild reduction (1 cm H₂O)
- EPR Level 2: Medium reduction (2 cm H₂O)
- EPR Level 3: Maximum reduction (3 cm H₂O)

![Diagram showing EPR levels and pressure profiles](image)

*ResMed Sleep Titration Guide 2013*
Recommendation: Position/Sleep Stage
(consensus)

• Ideally at least 15 min of supine REM sleep
• Patient may be awakened to reposition
• Increased sleep efficiency during the titration may predict long term adherence, therefore the decision to awaken the patient must be carefully considered
Recommendation: O₂

(consensus)

- Baseline, awake supine SpO₂ ≤88%
- SpO₂ ≤88% for >5 min in the absence of obstructive respiratory events
- Start with 1 LPM, goal SpO₂ 88-94%
- Effective O₂ concentration varies with mask leak, respiratory pattern
- Connect to the PAP device outlet
- Weaning down of O₂ by employing BiPAP or further increasing IPAP can be attempted

Medicare Coverage Criteria – $O_2$

- Oxygen not covered as a treatment for OSA
- Oxygen is covered for OSA patients with co-existing chronic pulmonary disease when...
  - $O_2 < 88\%$ for more than five minutes total at an effective PAP setting
  - PAP titration to an AHI $<10$ events/hour
- Only testing with a titration PSG may be used to qualify a beneficiary with OSA for concurrent payment of home oxygen (home oximetry will not do it)
Recommendation: F/U
*(standard)*

- PAP usage should be objectively monitored to help assure utilization
- Troubleshooting of problems encountered while on PAP, management of side-effects, and methods to increase adherence should be a part of the close follow-up of the patient on PAP
  - First few weeks are critical
  - Office visits
  - telemedicine

*Clinical Guidelines for the Manual Titration of Positive Airway Pressure, JCSM, 2008*
Predictors of PAP Adherence

- Disease and symptom severity
- Side effects and complaints
  - Inconvenience
  - Mask fit, comfort
- Psychological factors
  - Apprehension
  - Perceived benefit to patient and partner
  - Comorbid anxiety/depression
  - Sleep status (bed partner vs alone)
  - Socioeconomic status
- Early experience, education and support
  - Hypnotics
  - Early intervention
  - Objective monitoring (data cards, modem)
- Improving technologies

Catcheside, Medicine Reports 2010
Sleep During Titration Predicts Subsequent CPAP usage

Figure 1—Mean ± SEM objective compliance (hours per night) in individuals whose sleep efficiency improved from diagnostic to titration night and individuals whose sleep efficiency did not improve from diagnostic to titration night. CPAP=continuous positive airway pressure

Table 1—Mean ± SD of polysomnographic and self-report variables during screening and titration nights

<table>
<thead>
<tr>
<th>Sleep Parameter</th>
<th>Diagnostic</th>
<th>Titration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep Efficiency</td>
<td>81.45 ± 13.67</td>
<td>80.26 ± 12.16</td>
</tr>
<tr>
<td>Total Sleep Time (hours)</td>
<td>6.50 ± 1.10</td>
<td>6.41 ± 1.07</td>
</tr>
<tr>
<td>Latency to Stage 1 (min)</td>
<td>12.68 ± 25.65</td>
<td>13.92 ± 24.79</td>
</tr>
<tr>
<td>Latency to Persistent sleep (min)</td>
<td>27.83 ± 34.68</td>
<td>26.40 ± 29.87</td>
</tr>
<tr>
<td>Stage 1 Sleep (%)</td>
<td>31.19 ± 19.75</td>
<td>18.16 ± 9.26*</td>
</tr>
<tr>
<td>Stage 2 Sleep (%)</td>
<td>50.42 ± 15.89</td>
<td>55.25 ± 12.55*</td>
</tr>
<tr>
<td>Stage 3 and 4 Sleep (%)</td>
<td>5.95 ± 8.62</td>
<td>6.24 ± 7.84</td>
</tr>
<tr>
<td>REM Sleep (%)</td>
<td>12.77 ± 5.58</td>
<td>19.10 ± 8.93*</td>
</tr>
<tr>
<td>RDI</td>
<td>62.02 ± 32.20</td>
<td>6.06 ± 6.32*</td>
</tr>
<tr>
<td>O₂ Saturation Below 85% (#)</td>
<td>83.68 ± 144.21</td>
<td>7.29 ± 17.59*</td>
</tr>
<tr>
<td>Subjective Sleep Quality</td>
<td>2.87 ± .82</td>
<td>3.32 ± 1.03*</td>
</tr>
<tr>
<td>Subjective Depth of Sleep</td>
<td>2.87 ± .83</td>
<td>3.31 ± 1.04*</td>
</tr>
<tr>
<td>Subjective Total Sleep Time</td>
<td>7.08 ± 1.62</td>
<td>7.04 ± 1.99</td>
</tr>
</tbody>
</table>

* p < .05; RDI = Respiratory Disturbance Index (apneas + hypopneas/ hour of sleep); REM = rapid eye movement; for Likert measures (ie, quality and depth of sleep) higher scores indicate higher levels of each variable.
Sedative Use During the Titration

### Table 2—CPAP Titration Quality*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Eszopiclone Group (n = 50)</th>
<th>Placebo Group (n = 48)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep latency, min</td>
<td>19.4 ± 16.1</td>
<td>31.8 ± 30.4</td>
<td>0.08</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>87.8 ± 5.9</td>
<td>80.1 ± 10.5</td>
<td>0.002</td>
</tr>
<tr>
<td>WASO, min</td>
<td>39.3 ± 20.9</td>
<td>59.9 ± 31.5</td>
<td>0.009</td>
</tr>
<tr>
<td>TST, min</td>
<td>350.9 ± 33.6</td>
<td>319.7 ± 48.7</td>
<td>0.007</td>
</tr>
<tr>
<td>Total arousal index, events/h</td>
<td>19.2 ± 10.6</td>
<td>26.6 ± 17.1</td>
<td>0.04</td>
</tr>
<tr>
<td>AHI at highest CPAP, events/h</td>
<td>6.4 ± 7.0</td>
<td>12.8 ± 14.6</td>
<td>0.08</td>
</tr>
<tr>
<td>CPAP prescription, cm H₂O</td>
<td>9.1 ± 2.3</td>
<td>9.1 ± 1.4</td>
<td>0.99</td>
</tr>
</tbody>
</table>

*Values are given as the mean ± SD, unless otherwise indicated.

### Table 3—CPAP Compliance*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Eszopiclone Group (n = 50)</th>
<th>Placebo Group (n = 48)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of CPAP use, %</td>
<td>75.9 ± 20.0</td>
<td>60.1 ± 24.3</td>
<td>0.005</td>
</tr>
<tr>
<td>CPAP use per night on all nights, h</td>
<td>4.0 ± 1.6</td>
<td>2.9 ± 1.9</td>
<td>0.03</td>
</tr>
<tr>
<td>CPAP use per night on nights used, h</td>
<td>4.8 ± 1.5</td>
<td>3.9 ± 1.8</td>
<td>0.03</td>
</tr>
<tr>
<td>Nights with &gt; 4 h of CPAP use, %</td>
<td>59.2 ± 28.7</td>
<td>37.0 ± 30.8</td>
<td>0.007</td>
</tr>
<tr>
<td>Good compliance, %†</td>
<td>53.1 ± 49.8</td>
<td>27.1 ± 39.5</td>
<td>0.009</td>
</tr>
</tbody>
</table>

*All values are given as the mean ± SD, unless otherwise indicated.
†CPAP used for > 4 h/night on > 70% of nights.
An Oral Hypnotic Medication Does Not Improve Continuous Positive Airway Pressure Compliance in Men With Obstructive Sleep Apnea

Chest. 2006;130(5):1369-1376. doi:10.1378/chest.130.5.1369

Entry Criteria:
- Age ≥18
- Apnea/hypopnea Index ≥ 5
- Epworth Sleepiness Scale ≥ 10
- In-lab CPAP titration
- Agree to use nasal CPAP

Informed Consent Signed

72 patients randomized

Zolpidem 10 mg x 14 days (N = 24)
- + nCPAP
  - Follow-up after day 28
  - Pill count
  - ESS
  - FOSQ
  - CPAP data downloaded

Placebo pill x 14 days (N = 24)
- + nCPAP
  - Follow-up after day 28
  - Pill count
  - ESS
  - FOSQ
  - CPAP data downloaded

Standard Treatment (no zolpidem or placebo pill) (N = 24)
- + nCPAP
  - Follow-up after day 28
  - Pill count
  - ESS
  - FOSQ
  - CPAP data downloaded

Bradshaw, et al, 2006
Autotitrating CPAP (APAP) (standard)

• Not recommended to diagnose OSA
• Not recommended for….  
  – CHF  
  – COPD or other chronic lung disease  
  – Hypoxemia not due to OSA (eg OHVS)  
  – Non-snorers (natural or post surgery)  
  – Central sleep apnea syndromes

• Not recommended for split-night titrations

AASM Practice Parameter for Auto-CPAP, 2008
Autotitrating CPAP (APAP)

(guideline)

• Certain APAP devices may be used during attended polysomnography to identify a single pressure for use with standard CPAP for treatment of moderate-severe OSA

• Use of percentile measures to determine effective pressure levels may have inherent limitations and be device specific

AASM Practice Parameter for Auto-CPAP, 2008
Autotitrating CPAP (APAP) (option)

- Certain APAP devices may be initiated and used in the self-adjusting mode for unattended treatment of patients with moderate-severe OSA without significant comorbidities (e.g. CHF, COPD, CSA, hypoventilation syndromes)
- Certain APAP devices may be used in an unattended way to determine a fixed CPAP treatment pressure for patients with moderate-severe OSA without significant comorbidities (e.g. CHF, COPD, CSA, hypoventilation syndromes)

AASM Practice Parameter for Auto-CPAP, 2008
Autotitrating CPAP (APAP)
(standard)

- Patients being treated with fixed CPAP on the basis of APAP titration must have close clinical follow up to determine treatment effectiveness and safety. This is especially important during the first few weeks of PAP use.

- Reevaluation and, if necessary, a standard attended CPAP titration should be performed if symptoms do not resolve or if the APAP treatment otherwise appears to lack efficacy.

AASM Practice Parameter for Auto-CPAP, 2008
Titration Tips

• Mask fit and comfort are essential – take your time
• Keep the dentures in
• Don’t give up on a nasal mask too soon; use a chinstrap
• Record a brief entry with each pressure change
• Make sure you know the patient’s preferred body position and let them know they will be asked to sleep supine
• Distinguish phasic REM respiratory changes from apnea/hypopnea
• Avoid titrating sleep onset events
• Central apneas associated with loud snoring and/or are highly positional may be caused by airway obstruction - keep titrating
• Use expiratory relief technology
• Be prepared – CPAP, BiPAP, oxygen, ASV
• Post titration questionnaire
Phasic REM Sleep Respiratory Variability
Sleep Onset/Post Arousal Central Apnea
Recommendation: ASV

(consensus)

• Consider for Cheyne-Stokes respiration or if treatment emergent central sleep apnea is not eliminated by down titration of pressure
Sleep Related Breathing Disorders

• Central Sleep Apnea Syndromes
  – Central Sleep Apnea with Cheyne-Stokes Breathing (786.04/R06.3)
  – Central Sleep Apnea Due to a Medical Disorder without Cheyne-Stokes Breathing (327.27/G47.37)
  – Central Sleep Apnea Due to High Altitude Periodic Breathing (327.22/G47.32)
  – Central Sleep Apnea Due to a Medication or Substance (327.29/G47.39)
  – Primary Central Sleep Apnea (327.21/G47.31)
  – Primary Central Sleep Apnea of Infancy (770.81/P28.3)
  – Primary Central Sleep Apnea of Prematurity (770.82/P28.4)
  – Treatment Emergent Central Sleep Apnea (327.29/G47.39)
Sleep Related Breathing Disorders

• Sleep Related Hypoventilation Disorders
  – Obesity Hypoventilation Syndrome (278.03/E66.2)
  – Congenital Central Alveolar Hypoventilation Syndrome (327.25/G47.35)
  – Late-Onset Central Hypoventilation with Hypothalamic Dysfunction (327.26/G47.36)
  – Idiopathic Central Alveolar Hypoventilation (327.24/G47.34)
  – Sleep Related Hypoventilation Due to a Medication or Substance (327.26/G47.36)
  – Sleep Related Hypoventilation Due to a Medical Disorder (327.26/G47.36)

• Sleep Related Hypoxemia Disorder (326.26/G47.36)
Central Apnea Syndromes

- Eucapnic/Hypocapnic (hyperventilation)
  - Primary CSA
  - Cheyne-Stokes Respiration
  - CSA due to medical disorder
  - High altitude periodic breathing
  - Treatment emergent CSA (complex sleep apnea)
  - Medication or substance use/abuse

- Hypercapnic (hypoventilation)
  - Central drive abnormalities
  - Neuromuscular disorders
  - Chest wall disorders
Apnea Threshold

- Level of $\text{PaCO}_2$ below which a central apnea occurs
- AT varies with state; increased in sleep
- Sleep wake transitions, sleep-onset or post-arousal
Apnea Threshold
Ventilatory Instability

• Any mechanical system that is regulated by feedback loops has the potential to become unstable

• Loop Gain

• Phase delay between effector portion of system (lungs) and sensors (CO₂ detection in carotid body and brainstem)
  – Always present
  – Exaggerated in heart failure
Loop Gain

VENTILATORY RESPONSE TO A DISTURBANCE

DISTURBANCE

Low loop gain (<0.5) leads to stable ventilation

High loop gain (>1.0) leads to unstable ventilation
Treatment-Emergent Central Sleep Apnea

*(Complex Sleep Apnea)*

- **Diagnostic Criteria**
- PSG shows $\geq 5$ predominantly obstructive respiratory events/hour
- PSG during use of PAP without a back-up rate shows significant resolution of obstructive events and emergence or persistence of central events
  - Central apnea/hypopnea index $\geq 5$
  - Central apnea/hypopnea index $\geq 50\%$ of total AHI
- Not explained by another CSA disorder (eg CSB, medication or substance)

ICSD, 3rd edition
Treatment-Emergent Central Sleep Apnea

• Associated features
  – High arousal index on PAP
  – AHI often higher during NREM than REM sleep
  – AHI reduced when N3 sleep achieved, recurs after arousal or sleep stage transition
  – Often report little benefit from treatment with CPAP
Treatment-Emergent Central Sleep Apnea

- **Demographics**
  - 2-20% on initial titration
  - Increased in patients with another cause of CSA
  - Often resolves on chronic CPAP; 2% persistent
  - Regional differences?

- **Pathophysiology**
  - Low arousal threshold, high ventilatory controller gain
  - Excessive CPAP pressure, inadequate CPAP pressure
  - Reported following upper airway surgery and oral appliance use
Treatment Emergent Central Sleep Apnea

• Usually resolves with CPAP (weeks-months)
• ASV
  – Must have an effective EPAP
  – Continually adjusting pressure support to stabilize ventilation
  – Back up rate
Treating periodic breathing

- VPAP Adapt turned ON
- A decrease in ventilation is rapidly treated by increasing Pressure Support
- The minimal Pressure Support during normal breathing or hyperventilation prevents over ventilation and hypoxia
- VPAP Adapt turned OFF

VPAP Adapt rapidly stabilizes breathing by increasing Pressure Support in response to hypoventilation
Pressure Support decreases when normal breathing (or hyperventilation) resumes

ASVAuto mode

- Pressure Support increases as minute ventilation drops below the dynamic target during flow limitation
- Pressure Support increases as minute ventilation drops below the dynamic target during the obstructive apnea

- Increase in EPAP in response to flow limitation
- Increase in EPAP in response to obstructive apnea

ResMed Sleep Lab Titration Guide
Baseline flow

Recognizes decrease

Responds by increasing pressure support to bring flow waveforms up to previous levels