APAP: The Good, the Bad, the Ugly

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<th>Type of Potential Conflict</th>
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<td>Grant/Research Support</td>
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OBJECTIVES

1. Understand how AutoPAP works
2. Understand the difference between autoPAP and CPAP
3. Recognize the limitations and contra-indications to APAP use
4. Identify the clinical indications for APAP use
5. Utilize the appropriate PAP therapy (autoPAP vs CPAP) in the appropriate clinical setting
Understanding PAP therapy
CPAP Basic Overview

CPAP Therapy
A potential life saving and changing option for the treatment of sleep apnea.
Inside a CPAP machine
CPAP – The basics
Anatomy of a CPAP machine
Fundamentals of AUTO-PAP

- Whereas CPAP sends a fixed constant pressure, APAP fluctuates pressures based on airflow (inspiratory flow limitation, snoring, and apneas)
Conventional PAP therapy

- **Goal**: identify single effective pressure that will prevent all apnea, hypopnea, snoring, and respiratory effort-related arousals (RERAs) in all body positions and all sleep stages.

- Generally, higher pressures are needed in the supine position and during REM sleep.

- Higher pressures may also be needed to eliminate residual snoring and RERAs associated with airflow limitation than to prevent apnea and hypopnea.
Fundamentals of AUTO-PAP

- **Goal of APAP:** Provide the minimal effective pressure in a given circumstance

- **Most APAP devices measure (1 or more):**
  - snoring (airway vibration)
  - airflow (apnea or hypopnea)
  - flow vs. time profile (evidence of flattening as a surrogate for airflow limitation)

- **Changes in airflow may be detected by:**
  - Built-in pneumotachograph to quantify flow and the flow versus time profile
  - Differences in blower speed during inspiration and exhalation

- **Different manufacturers use differing PROPRIETARY algorithms to guide their APAP adjustments.**
  - E.g., S9 Autoset monitors breath-for-breath and takes a 5-breath average
AUTO-PAP Titrations

• Most APAP devices start with a baseline pressure then titrate upward as needed.
  • Increase pressures (per algorithm) if respiratory events detected
  • Reduce pressures if no events detected for set period of time, per algorithm

• An absence of monitored events then prompts a gradual decrease in pressure, which allows the minimum effective pressure to be delivered in a given circumstance.

• The clinician sets the maximum and minimum pressure limits.
Some machines are able to differentiate central apneas from obstructive apneas
Respironics Air Puff Technology

OBSTRUCTED AIRWAY
Respironics CSAD Accuracy

ResMed Forced Oscillatory Technique
ResMed Forced Oscillatory Technique
Accuracy of ResMed’s CSAD

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<th>Table 1. Sensitivity and specificity for CSAD</th>
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<td>Sensitivity</td>
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Defining Respiratory Events

- PSG uses airflow in combination with EEG, SpO2 and effort belts to measure AHI per hour of SLEEP

  vs

- PAP devices ONLY use airflow to define apneas and hypopneas per hour of DEVICE USE
Respiratory events recorded in PAP machines are NOT THE SAME as the respiratory events scored in PSGs!
Accuracy of APAP Automatic Event Detection

Agreement for AI was good, but less agreement with hypopnea scoring

Event-by-event comparison of manually scored PSG and AED events

Figure 4—In this 120-sec PSG tracing in Stage N2, the period of reduced airflow is detected as a hypopnea (H) event by AED but was not scored manually because it was not associated with a ≥ 4% decrease in oxygen saturation. Inspiration for the PAP flow signal (CFlow) is downward. The frequent narrow events on the AED signal are snoring. Here (H) marks the event detection signal for hypopnea and the corresponding airflow tracing event. The background “2” refers to stage N2.

Figure 5—A 120-sec PSG tracing in which a reduction in airflow with an associated 4% oxygen desaturation is scored manually as a hypopnea but did not trigger an AED hypopnea detection as the decrease in airflow during the event and increase in recovery airflow were not very large. In the event channel, the frequent narrow square waves were snoring events. Inspiration for the PAP flow signal (CFlow) is downward. The background “R” refers to stage R.

Take Home Points

• Event-by-event analysis showed that AED detection had a high specificity but only modest sensitivity (high number of false negatives).

• AHI < 10 events/hr by AED was highly predictive that the manually scored PSG AHI was < 10 events/hr.

• AHI ≥ 10 events/hr by AED was only moderately predictive that the PSG AHI was ≥ 10 events/hr (positive predictive value = 67%).

• AED tends to overestimate the AHI at low AHI values and underestimate the AHI at higher AHI values.

Clinical Use of APAP Algorithms

- AED algorithm has the greatest clinical utility when the residual AHI is low.
  - An AHI < 10 events/hr by AED is likely to indicate efficacious treatment.
  - High AHI values by AED may represent inadequate treatment especially if the reported events are apneas.

AED results must be combined with clinical assessment of the patient to determine appropriate management decisions.
Efficacy of APAP in the Treatment of OSA
Clinical Outcomes: APAP vs CPAP

<table>
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<tr>
<th>Parameter</th>
<th>APAP</th>
<th>CPAP</th>
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<tbody>
<tr>
<td>Reduction in AHI to acceptable levels*</td>
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<tr>
<td>Improvement in sleep quality</td>
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<td>Improvement in daytime sleepiness, as measured by decrease in ESS</td>
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<td>Improvement in daytime sleepiness, as measured by increase in MSLT</td>
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<td>Improvement in daytime sleepiness, as measured by increase in MWT</td>
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<td>Correction of oxygen desaturation related to OSA**</td>
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* APAP reduces the AHI to acceptable levels (AHI <10/hr) in greater than 80% - 95% of the OSA patients, and therapy with APAP and fixed CPAP appear to give similar treatment night AHIs.

** Though there may be a tendency for a lower minimum SaO2 on APAP than on fixed CPAP, though not clinically significant

Tolerance: APAP vs CPAP

- Twenty-nine patients with newly diagnosed mild to moderate OSAS (apnea-hypopnea frequency of 5-30 events/hour)
- Patients spent 8 weeks on continuous positive airway pressure (CPAP) and 8 weeks on APAP in a randomized crossover design.
- Setting: Respiratory Sleep Disorders Unit in a University Hospital and the patient’s home.
- Findings:
  - No significant differences in PSG or ESS, but all variables were significantly improved from baseline
  - Mean APAP pressure levels were significantly lower than CPAP (6.3 ± 1.4 vs 8.1 ± 1.7 cm H2O, p < .001).
  - More patients requiring higher fixed pressure (≥ 8cm H2O) preferred APAP, whereas those requiring lower pressure (< 8 cm H2O) preferred CPAP (p = 0.03)

Nolan GM; Doherty LS; Mc Nicholas WT. Auto-adjusting versus fixed positive pressure therapy in mild to moderate obstructive sleep apnoea. SLEEP 2007;30(2):189-194.
• 24 RCTs that compared APAP with fixed CPAP treatment in patients with OSA
• Fifteen trials used a cross-over design, nine a parallel design
• Mean baseline AHI ranged from 15 to 58 events/hour
• In all studies, most patients were either overweight or obese (BMI ranged from 29.9 to 42 kg/m2)
• None of the studies selectively focused on patients with other comorbidities
• Study durations ranged from three weeks to nine months, with the majority of studies lasting three months or less

• No statistically significant differences were observed in device usage (hours used per night) between APAP and CPAP in 20 of the trials, while four reported a significant increase in the use of APAP compared with CPAP.

• Meta-analysis showed statistically significant difference of **11 minutes per night favoring APAP** (difference = 0.18 hours; 95% CI, 0.05 to 0.31 minutes; P = 0.006)
Sixteen trials provided sufficient data for analysis of residual AHI while using treatment. None of the studies reported a statistically significant difference in AHI (events/hour) between APAP and CPAP.

Meta-analysis across these studies indicated a **non-significant difference** between APAP and CPAP of 0.25 events/hour (95% CI, -0.16 to 0.66 events/hour; P = 0.23).
ESS: APAP vs CPAP

- 22 trials reported ESS after treatment. 20 trials reported no statistically significant differences in ESS between APAP and CPAP while 2 studies reported a significant decrease in ESS favoring APAP.
- Mean net difference in ESS across all studies ranged from -3.3 to 2.0, where negative values favor less sleepiness with APAP.
- 18 trials provided sufficient data for meta-analysis, which yielded a statistically significant difference between APAP and CPAP of -0.48 (95% CI, -0.81 to -0.15; P = 0.005), favoring APAP.
Arousal Index: APAP vs CPAP

- Meta-analysis of nine trials showed a non-significant difference in arousal index of -0.85 events/hour (95% CI, -2.2 to 0.5 events/hour; P = 0.23), favoring APAP.
Oxygen Saturation: APAP vs CPAP

Meta-analysis of nine trials showed a statistically significant difference in minimum oxygen saturation of -1.3% (95% CI, -2.2 to -0.4%; P = 0.003), favoring CPAP.
Blood Pressure: APAP vs CPAP

• Three trials reported changes in blood pressure.

• Two studies did not find significant differences in blood pressure changes between the APAP and CPAP groups.

• Based on the data reported in the third study, a significantly greater reduction in diastolic blood pressure (net difference = 8 mmHg; 95% CI, 4 to 11 mmHg; P < 0.001), but not systolic blood pressure (net difference = 6 mmHg; 95% CI, -1 to 13 mmHg; P = 0.09), was noted with CPAP compared to APAP.
Patients with severe OSA are at increased risk of fatal and non-fatal cardiovascular events

APAP does not significantly decrease BP, despite reductions in AHI and CRP

Limitations of APAP
Limited Safety Data in CoMorbid Conditions

• Limited to no studies on use of APAP in patients with:
  • Heart failure
  • Renal failure, especially on dialysis
  • Cardiac arrhythmias
  • Central nervous system disorders
  • Central sleep apnea syndromes
  • Hypoventilatory disorders, including those causing chronic hypoxemia
  • Chronic lung disease, including COPD
  • Neuromuscular disorders
  • Comorbid sleep disorders

• As safety of APAP is yet unclear in these conditions, it is currently recommended to avoid use of APAP in these conditions.
APAP & Complex Sleep Apnea

• Prevalence of complex apnea in APAP use is 9.1%.
• Higher median apnea-hypopnea, mixed apnea and central apnea indices noted at baseline in patients who developed CompSA
• Mean AHI only dropped from 52.7 to 39.9 per hour in CompSA patients, while it improved from 40.9 to 7.3 in patients without CompSA.
• Higher rates of comorbid heart failure and obstructive pulmonary disease noted in patients who developed CompSA

All AutoPAPs are not the same

- Monitoring airflow with a pneumotachograph is likely to detect more events than with a thermistor.
- APAP devices using vibration alone may fail to work in patients with prior upper airway surgery or persons with minimal snoring.
- APAP units monitoring flow or impedance may fail to titrate properly because of high mask leaks.
- Using flow alone may not result in recognition of respiratory effort related arousals.
When to use which therapy?
Limitations of Conventional CPAP therapy

• Access
  • Remote areas may have limited access to sleep centers
  • Sleep Centers may have back logs
• Expense (attended titrations more expensive)
• Time & labor intensive
  • One tech cannot monitor > 2 patients
  • Scoring may take 2-3 hours
Limitations of Conventional PAP therapy

• Optimal pressure effective in all situations may not be identified on a single study night

• Optimal pressure may be higher than necessary for much of the night, as the needed CPAP pressure can vary considerably with sleeping posture and sleep stage

• Use of a single higher pressure for the entire night could potentially increase mask leaks, mouth leaks, pressure intolerance, and theoretically reduce acceptance and adherence with CPAP treatment in some patients

• Optimal pressure could also change with time, secondary to multiple factors including weight gain and nasal congestion
However...

- Avoid use of APAP therapy in patients with clinically significant comorbidities:
  - Cardiovascular abnormalities (e.g., heart failure, arrhythmias)
  - Renal failure, especially on dialysis
  - Central nervous system disorders
  - Central sleep apnea syndromes
  - Hypoventilatory disorders (including obesity hypoventilation)
  - Chronic lung disease, including COPD
  - Chronic hypoxemia or oxygen dependence
  - Neuromuscular disorders
  - Other comorbid sleep disorders (Insomnia, RLS etc)

- APAP therapy may not work in patients who do not snore (either naturally or secondary to palatal surgery), as sensors and algorithms identifying respiratory events may not be sensitive or specific under these circumstances.
Possible Decision Tree for the Use of APAP in Clinical Practice

Patient newly diagnosed with OSA

- Is AHI > 15?
  - Yes → Co-morbid Medical Conditions
    - Moderate to Severe Lung Disease
    - Congestive Heart Failure
    - Oxygen Dependence
    - Hypoxemia (O2 Saturation < 90%)
    - Proprietary or Inherited Causes of OSA
    - Physical Inability or Intensive Issues
    - Neurologic or Neuromuscular Disease
    - Non-anatomic Obstructive Sleep Apnea
    - Parasomnia, restless leg syndrome
    - Sleep-Related Hypoxemia
  - No → Patient has a history of co-morbid medical conditions or sleep disorders?
    - Yes → Co-morbid Sleep Disorder
      - PLMD or periodic leg movements
      - Neurologic or Metabolic Hypoxemia
      - Moderate to Severe Obstructive Sleep Apnea
      - Personality or Neurochemical Factors
      - Central Sleep Apnea
      - Sleep-related Hypoxemia
    - No → Patient has undergone upper airway surgery?
      - Yes → Good candidate for empirical auto-CPAP (APAP), place an order for new set at 5 to 20 cm water with compliance download in 2 weeks.
      - No → Compliance review shows good compliance***, symptoms are improved and download AHI is less than 10.
  - No → Discuss treatment options (CPAP and alternative to PAP therapy)

Clinical Follow-up and Treatment as indicated

In clinical follow must occur for face to face visit within 31st to the 90th day of date of initial setup. Compliance download must be reviewed at each clinic visit whenever available. Clinical response to PAP therapy must be documented in the clinic visit notes.

*If the attended titration study is not approved by insurance, APAP treatment may be initiated.
** If an attended PSG is not approved initially and home study does not show OSA, an attended PSG should then be done to rule out persistent OSA.
***Use of APAP for > 10 % of the nights for more than 4 hours in a 24-hour period during a 30-consecutive day period.

(Reprinted with permission from Kaplish N, University of Michigan's Michael Aldrich Sleep Disorders Center)
Another Possible Cost Effective Decision Tree—Utilizing Home Sleep Testing

1. Administer the STOP BANG questionnaire
2. Determine the contraindications for portable monitoring (PM) study
3. Document upper airway anatomy

Patient presents with sleep apnea related symptoms

STOP BANG: high risk for SDB and no contraindications for PM
Order PM study

Study report confirms OSA; absence of CSA or severe hypoxemia
Order APAP per sleep study report (if there are no contraindications*)
Follow-up between 30-60 days of PAP use
Fails APAP/poor compliance despite intervention

Study report does not confirm OSA or shows CSA (CA≥5/hr)/severe hypoxemia
Follow-up in Sleep Clinic

STOP BANG high risk for SDB but there are contraindications for PM
Order full attended PSG, baseline/split-night study

Study report confirms OSA / CSA or hypoventilation and lab completes PAP titration
Order therapy based on sleep study results

Study report does not confirm SDB or suggests other sleep disorder(s) or STOP BANG was low risk
Summary
APAP & FCPAP Similar in Efficacy

• In patients with moderate to severe OSA without significant comorbidities, APAP and CPAP are similar in affecting relatively short-term changes in:
  • AHI
  • Arousal Index
  • Sleep efficiency
  • % of time in REM sleep
  • (+/- Slow wave sleep)
  • Quality of life
  • Unexpected adverse events
Mild Differences in Clinical Parameters

**APAP**
- Mildly better at improving daytime sleepiness than fixed CPAP (by ~ 0.5 points on ESS)
- Associated with mildly better compliance than fixed CPAP (by 11 minutes per night).

**Fixed CPAP**
- Mildly better at maintaining SpO2 (min SpO2 1.3% higher in fixed CPAP than APAP)
- Possibly better at reducing diastolic (but not systolic) BP (by 8 mmHg)

Clinical significance of these is unclear.
APAP and CPAP result in largely similar treatment effects for patients with OSA without significant comorbidities.
Modes of APAP therapy

- Fixed Pressure Therapy
  - Set at $P_{90}$, $P_{95}$, $P_{max}$, or based on titration
- Auto Adjusting Therapy
Clinical Efficacy of APAP therapy

• Effective APAP therapy requires:
  • Judicious patient selection for unattended APAP titration
  • Knowledgeable physician review of stored information for the APAP device
  • Timely follow-up of the outcome of CPAP treatment
  • Proper mask fitting and leak control are essential

• Unattended titration requires that the patient be well educated about using the device and be able to apply the mask properly and adjust it if leaks occur.
Data from the AAVA
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<td>Total pts</td>
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<tr>
<td>% of patients who are compliant with therapy (&gt; 4 hours/night for ≥ 70% of nights)</td>
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<tr>
<td>Average % of nights with &gt; 4 hours of use (of compliant patients)</td>
<td>87%</td>
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