Effect of continuous positive airway pressure on blood pressure in patients with minimally symptomatic obstructive sleep apnoea: a meta-analysis using individual patient data from four randomised controlled trials – Online supplement

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1. Search Strategy for MEDLINE
1   randomized controlled trial.pt
2   controlled clinical trial.pt
3   randomized.ab
4   placebo.ab
5   clinical trials as topic.sh
6   randomly.ab
7   trial.ti
8   1 or 2 or 3 or 4 or 5 or 6 or 7
9   apn$ea.af
10  OSAS.af
11  hypopnSea.af
12  SAHS.af
13  obstructive sleep apn$ea.af
14  9 or 10 or 11 or 12 or 13
15  CPAP.af
16  continuous positive airway pressure.af
17  15 or 16
18  Blood pressure.af
19  Minimally symptomatic.af
20  Non$sleepy.af
21  Non$symptomatic.af
22  Aymptomatic.af
23  19 or 20 or 21 or 22
24  8 and 14 and 17 and 18 and 23
## 2. Summary of CPAP adherence

<table>
<thead>
<tr>
<th>Trial</th>
<th>No. allocated to CPAP</th>
<th>Median usage (25&lt;sup&gt;th&lt;/sup&gt;, 75&lt;sup&gt;th&lt;/sup&gt; percentiles) (hours/night)</th>
<th>No. (%) using ≥4 hours/night</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barbé (2001)</td>
<td>29</td>
<td>5.1 (4.0, 6.5)</td>
<td>22 (76%)</td>
</tr>
<tr>
<td>Robinson (2006)</td>
<td>17</td>
<td>5.5 (4.4, 7.0)</td>
<td>14 (82%)</td>
</tr>
<tr>
<td>Barbé (2012)</td>
<td>358</td>
<td>5.0 (3.0, 6.3)</td>
<td>219 (61%)</td>
</tr>
<tr>
<td>Craig (2012)</td>
<td>195</td>
<td>2.5 (0.5, 4.9)</td>
<td>66 (34%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>599</strong></td>
<td><strong>4.7 (2.1, 6.0)</strong></td>
<td><strong>321 (54%)</strong></td>
</tr>
</tbody>
</table>

eTable 2.1 - Summary of adherence to CPAP

Summary of average adherence to CPAP (hours/night) and the proportion of participants using CPAP ≥4 hours/night in each study and overall. Average adherence for each patient is calculated as the total number of hours used divided by total number of days used over follow-up.
3. Effect of CPAP usage on secondary outcomes

eFigure 3.1: Forest plots showing the effect of less than and more than 4 hours/night CPAP usage on Epworth Sleepiness Score (ESS) compared to control in each study and overall. Difference between pooled treatment effects: p<0.001
eFigure 3.2: Forest plots showing the effect of less than and more than 4 hours/night CPAP usage on sleep apnoea severity (ODI/AHI, events/hour) in each study and overall
Difference between pooled treatment effects: p<0.001
4. Treatment interactions with binary baseline covariates

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment effect (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barbe (2001)</td>
<td>-2.3 (-22.6, 18.0)</td>
<td>2.82</td>
</tr>
<tr>
<td>Robinson (2006)</td>
<td>22.2 (-11.0, 55.5)</td>
<td>1.05</td>
</tr>
<tr>
<td>Barbe (2012)</td>
<td>-1.2 (-7.0, 4.6)</td>
<td>34.85</td>
</tr>
<tr>
<td>Craig (2012)</td>
<td>-0.9 (-5.2, 3.4)</td>
<td>61.28</td>
</tr>
<tr>
<td>Overall (I-squared = 0.0%, p = 0.596)</td>
<td>-0.8 (-4.2, 2.6)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Treatment-gender interaction on SBP (mmHg)

*p-value for overall interaction = 0.639

eFigure 4.1: Forest plot showing the difference in treatment effects on systolic blood pressure (SBP, mmHg) between males and females in each study and overall
Figure 4.2: Forest plot showing the difference in treatment effects on diastolic blood pressure (DBP, mmHg) between males and females in each study and overall.

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment effect (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barbe (2001)</td>
<td>3.9 (-11.4, 19.3)</td>
<td>2.24</td>
</tr>
<tr>
<td>Robinson (2006)</td>
<td>9.0 (-11.7, 29.8)</td>
<td>1.22</td>
</tr>
<tr>
<td>Barbe (2012)</td>
<td>-1.7 (-5.8, 2.4)</td>
<td>31.30</td>
</tr>
<tr>
<td>Craig (2012)</td>
<td>-0.2 (-3.0, 2.7)</td>
<td>65.24</td>
</tr>
<tr>
<td>Overall (I-squared = 0.0%, p = 0.676)</td>
<td>-0.4 (-2.7, 1.8)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Treatment-gender interaction on DBP
p-value for overall interaction = 0.703
Figure 4.3: Forest plot showing the difference in treatment effects on Epworth Sleepiness Score (ESS) between males and females in each study and overall

Treatment-gender interaction on ESS
p-value for overall interaction = 0.695
**eFigure 4.4:** Forest plot showing the difference in treatment effects on systolic blood pressure (SBP) between users and non-users of anti-hypertensive medication in each study and overall.
Figure 4.5: Forest plot showing the difference in treatment effects on diastolic blood pressure (DBP) between users and non-users of anti-hypertensive medication in each study and overall.
5. Treatment interactions with continuous baseline covariates

eFigure 5.1: Effect of CPAP on change in systolic BP (SBP) compared to control over the full range and in quartiles of observed baseline systolic BP

eFigure 5.2: Effect of CPAP on change in systolic BP compared to control over the full range and in quartiles of observed body mass index (BMI)
eFigure 5.3: Effect of CPAP on change in systolic BP (SBP) compared to control over the full range and in quartiles of observed baseline Epworth Sleepiness Score (ESS)

eFigure 5.4: Effect of CPAP on change in systolic BP (SBP) compared to control over the full range and in quartiles of observed baseline ODI/AHI (events/hour)
Figure 5.5: effect of CPAP on change in diastolic BP (DBP) compared to control over the full range and in quartiles of observed baseline DBP

p-value for interaction $p = 0.633$

Figure 5.6: effect of CPAP on change in diastolic BP (DBP) compared to control over the full range and in quartiles of observed BMI

p-value for interaction $p = 0.052$
eFigure 5.7: effect of CPAP on change in diastolic BP (DBP) compared to control over the full range and in quartiles of observed baseline Epworth Sleepiness Score (ESS)

p-value for interaction $p = 0.425$
**eFigure 5.8:** Effect of CPAP on change in diastolic BP (DBP) compared to control over the full range and in quartiles of observed baseline ODI/AHI (events/hour)

**eFigure 5.9:** Effect of CPAP on change in Epworth Sleepiness Score (ESS) compared to control over the full range and in quartiles of observed body mass index (BMI)