Device-guided breathing exercises for the treatment of hypertension: An overview

Kornelis JJ van Hateren, Gijs WD Landman, Susan JJ Logtenberg, Henk JG Bilo, Nanne Kleefstra

Abstract

The American Heart Association considers device-guided breathing as a reasonable treatment modality in their statement on non-pharmacological options for lowering blood pressure. This review discusses all randomized controlled trials that have investigated the effects of device-guided breathing on blood pressure in patients with hypertension. Thirteen studies were included in this review. In total, 627 patients were included, of which 365 patients were allocated to device-guided breathing. Only 6 studies used acceptable control groups: listening to music, meditative relaxation exercises, or a sham-device. Two sponsored trials showed beneficial effects of device-guided breathing, both used listening to music as a control group. The remaining 4 studies, which had no employees of the manufacturer listed as co-author, observed no beneficial effects on blood pressure. There is only 1 study that used a sham device as a control group. All other studies were to some extend methodologically flawed. Based on the studies with an acceptable methodological quality, there is no clear evidence supporting a short-term beneficial effect on blood pressure by using device-guided breathing.

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Key words: Hypertension; Device-guided breathing; Review

Core tip: This review discusses all randomized controlled trials that have investigated the effects of device-guided breathing on blood pressure. There were 6 studies with an acceptable control group. Two (manufacturer sponsored) trials showed beneficial effects of device-guided breathing, both used listening to music as a control group. The remaining 4 studies observed no beneficial effects. We conclude that there is no sufficient evidence for recommending device-guided breathing in the treatment of hypertension.


INTRODUCTION

Treatment of hypertension includes both pharmacological and non-pharmacological interventions. Accepted non-pharmacological interventions are sodium restriction, losing weight, increasing physical activity, smoking cessation and optimizing alcohol consumption. In a scientific statement from the American Heart Association
tion (AHA) regarding non-pharmacological options for lowering blood pressure, device-guided slow breathing is described as a reasonable treatment modality to reduce blood pressure (Class II A, Level of Evidence B)[6]. Device-guided slow breathing aims at lowering the respiratory frequency into a so-called “therapeutic breathing zone” (less than 10 breaths per minute) through biofeedback by using an electronic device. Exercises are regarded as successful if the total exercise time is at least 45 min per week, preferably 15 min daily[8]. Sympathetic overactivity is hypothesized as an important contributing factor in the development of hypertension[67]. Efforts aimed at reducing this autonomic imbalance may indeed be an effective therapy for hypertension. Slow and regular breathing, guided by musical tones, will lead to a reduction of sympathetic activity and also to an increase in heart rate variability[25]. The baroreceptors measure blood pressure in the carotid arteries and the aorta, and an increase in pressure leads to parasympathetic activation and vice versa (negative feedback mechanism). As an increase in heart rate variability will lead to an increased baroreflex sensitivity[9], device-guided breathing may lead to lower blood pressure values.

The conclusions of the writing group of the AHA statement were based on a meta-analysis[8] and several other studies[9,10]. After the publication of the guideline, two additional studies have been published[20,21]. The overall effect estimate in the meta-analysis showed a small beneficial blood pressure lowering effect [a reduction of 3.7 mmHg in systolic blood pressure (SBP), but the authors of the meta-analysis stated that the results of the overall effect estimates should be interpreted with caution because of methodological flaws in most studies. Beneficial effects were not observed after excluding studies with high risk of bias or studies that were sponsored by or involved the manufacturer of the device[9]. A previous editorial already emphasized that an independent double-blind study with a proper control group, preferably a sham device, would be necessary to answer the question whether device-guided breathing has any effect on blood pressure[25]. Recently, an investigator-initiated double-blind and sham-controlled trial was performed[28]. This review discusses all randomized controlled trials (RCTs) that have investigated the effects of device-guided breathing on blood pressure in patients with hypertension.

PREVIOUS STUDIES

Thirteen studies, of which the study and patient characteristics are presented in Table 1, were included in this review. In total, 627 patients were included, of which 365 patients were allocated to device-guided breathing. Except for 1 study in which a bi-level positive pressure device (BiPAP®) was used[19], all other studies used the Resperate® device. The Resperate® device uses a form of biofeedback with “breathe in” and “breathe out” instructions according to the listeners breathing rate to guide the respiration into a lower frequency by prolonging expiration. The BiPAP® device was used for the treatment of patients with obstructive sleep apnea and it was also capable of guiding patients’ respiratory rate to less than 10 breaths per minute. Three studies had no control group[11,12,19], 4 studies compared the intervention to usual care or frequent blood pressure measurements[13,14,17,21], 4 studies compared the intervention to listening to music[9,10,15,16], 1 study compared the intervention to meditative relaxation exercises[19], and 1 study used a sham-device in the control group[20]. Except for 3 studies[11,12,20], all other studies were sponsored by or involved the manufacturer of the Resperate® and BiPAP® devices. According to the meta-analysis by Mahtani et al[8], the Anderson paper was also not sponsored by the manufacturer[10]. However, the acknowledgements section of this manuscript states that Drs. B. Gavish, an employee of the company that manufactures the Resperate® device, had reviewed the paper.

EFFECTS OF DEVICE-GUIDED BREATHING

Table 1 presents an overview of the effects of device-guided breathing on blood pressure. Only 4 studies reported between-group-differences including the 95% confidence intervals[9,10,15,16]. Significant decreases in blood pressure were observed in all 3 studies without a control group[11,12,19]. A significant between-group-difference was observed in 2 out of 4 studies that compared device-guided breathing to usual care or frequent blood pressure measurements[13], and usual care[17]. Studies comparing device-guided breathing to usual care cannot differentiate the 3 possible mechanisms through which the Resperate® could have a blood pressure lowering effect: (1) effects of guided slowing of breathing itself; (2) listening to music; and (3) sitting still. Conclusions regarding the isolated effect of device-guided breathing are only valid when a study has an appropriate control group to disentangle these 3 effects. Therefore, this review will further focus on the 6 studies that used acceptable control groups: listening to music, meditative relaxation exercises and a sham-device[9,10,15,16,18,20]. Two sponsored trials showed beneficial effects of device-guided breathing, both used listening to music as a control group[9,10]. In the study by Schein et al[9] device-guided breathing was not effective in lowering SBP compared to the control group. This study pre-defined a 5 mmHg reduction in diastolic blood pressure (DBP) as clinically relevant. The difference in DBP change between both groups was 4.4 mmHg in favour of the intervention group (P = 0.008). Although a second study failed to predefine a clinically relevant difference, it showed a significant decrease in office SBP compared to a Walkman group (between-group-difference 4.6 mm Hg, P = 0.001)[9]. The remaining 4 studies, which had no employees of the manufacturer listed as co-author, observed no beneficial effects on blood pressure[15,16,18,20]. Only the study by Landman et al[20] described the presence of 2 negative side-effects, but this was insufficient to conclude
that there was a causal relationship with device-guided breathing.

**METHODOLOGICAL QUALITY**

In order to compare the studies, we assessed the methodological quality using the criteria as described by van Tulder et al.[13] (Table 2). The quality of the study by Anderson et al. was low; they used an open randomisation procedure without any further explanation regarding this procedure and blinding.[15]. After carefully evaluating the studies by Schein et al.[10] and Grossman et al.[11] several methodological questions remained unanswered. It was stated in the Schein et al.[10] study that the study had a double-blind study design[10]. Randomisation was performed by a third party and a special technician delivered and

Table 1  Study and patients characteristics

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Study group</th>
<th>Disease, therapy, patients</th>
<th>Number (I/C)</th>
<th>Period (wk)</th>
<th>Study arm</th>
<th>Intervention</th>
<th>Control</th>
<th>Endpoint</th>
<th>Results (mean)</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td>Intervention (mmHg)</td>
</tr>
<tr>
<td>Schein et al.[10], 2001; Israel</td>
<td>HT, medication, BP ≥ 140/90, 25-75 yr</td>
<td>32/33</td>
<td>8</td>
<td>Resperate®</td>
<td>15 min/d</td>
<td>Walkman</td>
<td>SBP</td>
<td>156.6 &gt; 141.4</td>
<td>154.7 &gt; 143.4</td>
</tr>
<tr>
<td>Israel</td>
<td>Grossman et al.[11], 2001; Israel</td>
<td>BP ≥ 140/90, 25-75 yr</td>
<td>18/15</td>
<td>8</td>
<td>Resperate®</td>
<td>10 min/d</td>
<td>Walkman</td>
<td>DBP</td>
<td>95 &gt; 91</td>
</tr>
<tr>
<td>Rosenthal et al.[12], 2001; Israel</td>
<td>HT, medication, BP ≥ 140/90, 25-75 yr</td>
<td>13/-</td>
<td>8</td>
<td>Resperate®</td>
<td>24 h</td>
<td>15 min/d</td>
<td>SBP</td>
<td>137.1 &gt; 129.9</td>
<td>-</td>
</tr>
<tr>
<td>Viskoper et al.[13], 2003; Israel</td>
<td>HT, medication, SBP 140-160 or DBP 90-100, 40-80 yr</td>
<td>17/-</td>
<td>8</td>
<td>Resperate®</td>
<td>15 min/d</td>
<td>-</td>
<td>Home, SBP</td>
<td>82.5 &gt; 80.2</td>
<td>-</td>
</tr>
<tr>
<td>Meles et al.[14], 2004; Italy</td>
<td>HT, 40-75 yr + 1) not treated, SBP 140-159 or DBP 90-99; OR = 2) medication and BP ≥ 140/90</td>
<td>48/31</td>
<td>8</td>
<td>Resperate®</td>
<td>15 min/d</td>
<td>BP 1/d</td>
<td>Home, SBP</td>
<td>137 &gt; 131.6</td>
<td>126 &gt; 124.1</td>
</tr>
<tr>
<td>Elliot et al.[15], 2004; United States</td>
<td>HT, medication, SBP 140-179, DBP &lt; 110, 40-75 yr</td>
<td>89/60</td>
<td>8</td>
<td>Resperate®</td>
<td>15 min/d</td>
<td>BP 3/d</td>
<td>Clinic, SBP</td>
<td>105.3 &gt; 139.7</td>
<td>149.8 &gt; 140.6</td>
</tr>
<tr>
<td>Logtenberg et al.[16], 2007; The Netherlands</td>
<td>T2DM, HT, medication, SBP 140-160, 18 yr</td>
<td>15/15</td>
<td>8</td>
<td>Resperate®</td>
<td>15 min/d</td>
<td>Discman</td>
<td>Clinic, SBP</td>
<td>83.0 &gt; 82.0</td>
<td>87.0 &gt; 81.5</td>
</tr>
<tr>
<td>Altena et al.[17], 2008; The Netherlands</td>
<td>HT, medication, SBP 140-160, 18 yr</td>
<td>15/15</td>
<td>8</td>
<td>Resperate®</td>
<td>15 min/d</td>
<td>Discman</td>
<td>Clinic, SBP</td>
<td>9.8 &gt; -5.6</td>
<td>4.2 (-12.4-3.9)</td>
</tr>
<tr>
<td>Schein et al.[10], 2009; Israel</td>
<td>T2DM, HT, medication, SBP &gt; 130 Stage 1 HT or pre-hypertension, no medication, no CVD or T2DM.</td>
<td>33/33</td>
<td>8</td>
<td>Resperate®</td>
<td>15 min/d</td>
<td>Usual care</td>
<td>Clinic, SBP</td>
<td>150 &gt; 140</td>
<td>147 &gt; 149</td>
</tr>
<tr>
<td>Anderson et al.[18], 2010; United States</td>
<td>HT and OSA, medication or untreated, BP 120/80-160/100, 20-75 yr</td>
<td>25/-</td>
<td>8</td>
<td>BiPAP®</td>
<td>15 min/d</td>
<td>Clinic, SBP</td>
<td>82.7 &gt; 80.2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Landman et al.[19], 2013; The Netherlands</td>
<td>T2DM, HT, medication, SBP 140-160, 18 yr</td>
<td>24/24</td>
<td>8</td>
<td>Resperate®</td>
<td>15 min/d</td>
<td>Sham- Device</td>
<td>Clinic, SBP</td>
<td>151.6 &gt; 145.6</td>
<td>151.2 &gt; 142.8</td>
</tr>
<tr>
<td>Howorka et al.[20], 2013; Austria</td>
<td>T2DM, HT, medication, BP &lt; target value, 18-78 yr</td>
<td>16/16</td>
<td>8</td>
<td>Resperate®</td>
<td>12 min/d</td>
<td>Usual care</td>
<td>Clinic, SBP</td>
<td>129.3 &gt; 127.1</td>
<td>?</td>
</tr>
</tbody>
</table>

*P < 0.05 vs control. I: Intervention; C: Control; HT: Hypertension; SBP: (Systolic) blood pressure; DBP: Diastolic blood pressure; T2DM: Type 2 diabetes mellitus; CVD: Cardiovascular disease; OSA: Obstructive sleep apnea.*
explained the device and study procedures. Although the
doctor was not aware of the group assignment, patients
had weekly follow-up meetings including blood pressure
measurements by that same person. Patients were
requested not to talk about the specific device with their
doctor or to other persons who may be participating in
the study. As the patients saw their doctor very regularly
it is not unlikely that the doctor became aware of group
assignment. Therefore, from a methodological point of
view, the authors could have opted for another person
performing the outcome measurements. An alternative
method would have been to check the success of the
blinding procedure. The authors did not explain their
rationale behind this randomisation procedure. Furthermore,
there were several primary endpoints instead of 1
primary endpoint and 2 secondary endpoints. Also, 5% of
all blood pressure data were excluded in an unconvention-
al and post-hoc defined 'end of treatment period' analysis.

Grossman et al[10] did not describe whether treat-
ment allocation was concealed and who performed the
outcome measurements. Also, data on compliance and
whether the blinding procedure was a success, were not
provided. Two patients in the control group started
lifestyle modification programmes, but analyses without
these patients did not change the results.

The Logtenberg, Altena et al[16] and Landman et al[20]
studies have one important limitation in common: the
width of the 95% CI of the change of office-measured
SBP between groups[9,16,20]. These studies were powered
to detect an absolute reduction of 10 mm Hg in SBP. In
all these studies the limits of the confidence intervals
exceeded the boundary of 10 mm Hg. The 95% CI in the
Logtenberg et al[15] and Landman et al[20] studies ranged
from -2.3 mmHg to 11.7 mm Hg, and -6.5 mm Hg to
11.2 mm Hg, respectively, with a direction in favour of the
control group[15,20]. This means that clinically relevant
disadvantageous effects of device-guided breathing could
not be ruled out. For the Altena et al[16] study, the con-
fidence interval ranged from -12.4 mmHg to 3.9 mmHg
with a direction in favour of the intervention group[16].
Logtenberg et al[15] did not provide data on avoiding co-
interventions, whereas Altena et al[16] reported that 1 patient
in the control group had a change in antihypertensive
therapy (per-protocol analyses showing the same results).

HbA1c level was higher in the intervention group of the
Landman et al study, but additional analyses in which
adjustments for age, gender, body mass index and HbA1c
were done did not relevantly change the results[20]. The
adjusted differences in SBP and DBP were 1.1 mmHg
(95% CI: -7.6-9.8, in favour of the control group) and 3.5
mmHg (95% CI: -0.4-7.4, in favour of the intervention
group), respectively. Finally, the Logtenberg et al[15] and
Altena et al[16] studies had a single-blind design.

Sample size calculations were described in 4 stud-
ies[9,13,16,20], and lacking in the Anderson et al[18] and Gross-
man et al[10] studies[9,16]. Although Grossman et al[10]
mentioned that the group size was large enough, they didn’t
provide a calculation[10]. The Logtenberg study based the
calculation on mean SBP and standard deviation (SD) in
their clinic[15]. Altena et al[16] used the mean blood pres-
sure and SD that were observed in the Logtenberg et al[15]
study. The most conservative and optimal calculation
was performed in the Landman study, as they based their
sample size on the highest SD of the change in SBP in
the Logtenberg et al[15] (SD 9.4 mmHg) and Altena et al[16]
(SD 10.9 mm Hg) studies[20]. Comparable to their data
analysis, Schein et al[9] used an unconventional method for
the estimation of their sample size. The standardised de-
tectable difference was based on a previous study[24]
while they could have used the change in blood pressure and its
SD.

DISCUSSION

Out of the 13 RCTs published, there were only a few
studies with an acceptable methodological quality. All
studies had a short follow-up period. In order to exert ef-
effects on cardiovascular morbidity by using device-guided
breathing, the device has to be used for many months
and preferably years. None of the studies investigated
whether the device could be used for prolonged periods.
There is 1 meta-analysis, without any involvement of
the manufacturer, that showed a small beneficial effect
on blood pressure with unclear clinical relevancy of
using device guided breathing[8]. As was discussed by
the authors of this meta-analysis, the overall effect estimate
could have been biased due to inclusion of inadequately
controlled trials and sponsored studies. In studies with

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Table 2  Randomized controlled trials with an active control group: methodological quality

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<tbody>
<tr>
<td>Randomization adequate</td>
<td>*/-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Treatment allocation concealed</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Groups similar at baseline</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Patient blinded</td>
<td>*/-</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Care provider blinded</td>
<td>*/-</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Outcome assessor blinded</td>
<td>-</td>
<td>?</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Co-interventions avoided</td>
<td>+</td>
<td>-/+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Compliance acceptable</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Withdrawal/drop-out rate accept</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Timing of outcome assessment similar</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Intention to treat analyses</td>
<td>*/-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>
CONCLUSION

We conclude that, based on studies with acceptable methodological quality, there is no evidence for a short-term beneficial effect on blood pressure by using device-guided breathing. A meta-analysis of individual patient data combining studies with adequate control groups should be performed in the near future. Since there are no trials, not even uncontrolled, with sufficient follow-up on the feasibility and safety of using the device for many months or years, this device cannot safely be advised for treating hypertension in daily practice.

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