



Device-guided breathing: an effective treatment for high blood pressure in patients with diabetes mellitus?

"A relatively new intervention that is promoted as an addition to ... nonpharmacological options is treating hypertension with device-guided breathing exercises."

Hypertension and Type 2 diabetes mellitus (T2DM) are both important risk factors for cardiovascular disease, and the combination of both is even more deleterious than the separate disease entities. Aggressive treatment of hypertension is effective in reducing cardiovascular morbidity and mortality, and is therefore recommended for all patients with T2DM in various international guidelines [1–3]. Treatment of hypertension should include both pharmacological and nonpharmacological interventions. Accepted nonpharmacological interventions are sodium restriction, changing dietary habits, losing weight, increasing physical activity, smoking cessation and optimizing alcohol consumption [1–3]. A relatively new intervention that is promoted as an addition to these nonpharmacological options is treating hypertension with device-guided breathing exercises. This intervention aims at lowering the respiratory frequency into a so-called 'therapeutic breathing zone' (less than 10 breathings per minute) by using an electronic device. This device uses 'breathe in' and 'breathe out' tones to guide the respiration into a lower frequency, especially by prolonging expiration. Exercises are said to be successful if the total exercise time is at least 45 min per week, preferably 10–15 min daily [4–8].

The theory behind the efficacy of device-guided breathing is that slow and regular breathing, guided by slowing of musical tones, increases heart rate variability, which in turn increases baroreflex sensitivity [9]. Increase of baroreflex sensitivity is considered to reduce autonomic imbalance, which is hypothesized to be an important factor in the development of hypertension [9–11]. Until now, eight trials investigating device-guided breathing have been published [4–8,12–14]. Only two studies were performed in subjects with T2DM [13,14]. This editorial will discuss the current evidence for using device-guided breathing for the treatment of hypertension.

Six studies were performed in nondiabetic patients [4–8,12]. In total, 356 patients were included, of which 217 patients were allocated to use of the device. In all but one study a systolic blood pressure (BP) above 140 mmHg was an inclusion criterion. Two of these studies did not have a control group [6,7], two used self-measurement of BP as a control [8,12] and two studies used listening to music as a control [4,5]. In the study by Schein *et al.*, device-guided breathing was not effective in lowering systolic BP compared with the control group. The difference in diastolic BP change between both groups was 4.4 mmHg in favor of the intervention group ($p = 0.008$) [4]. The study by Grossman *et al.* was the only study in which a significant decrease in systolic BP was seen compared with the control group (between-group difference: 4.6 mmHg, $p = 0.001$) [5].

"[Device-guided breathing]... aims at lowering the respiratory frequency into a so-called therapeutic breathing zone."

The first trial performed in a diabetic population compared device-guided breathing to listening to music with a portable CD player during a period of 8 weeks ($n = 30$) [13]. In this study, the between-group difference for systolic BP proved to be 4.6 mmHg (95% CI: -2.3–11.7) in favor of the control group. These results are in contrast with those of a more recently published study that randomized between device-guided breathing and continuing usual care during a period of 8 weeks ($n = 71$) [14]. Systolic BP significantly decreased compared with the control group (between-group difference: 11.6 mmHg, $p < 0.0001$) [14]. In order to compare both studies, we assessed the methodological quality using the same criteria as described by van Tulder *et al.* [15]. Since both manuscripts were not conclusive regarding some items, the authors were asked for additional



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information. This allowed us the opportunity to discuss all quality criteria, pertaining to internal validity, for both studies.

Was the method of randomization adequate? Was the treatment allocation concealed?

In the Logtenberg *et al.* study, patients were randomized using sealed nontransparent envelopes. Patients were randomized in pairs of enrolled patients in the Schein *et al.* study. In order to maintain equal-size groups, patients who dropped out after randomization were automatically replaced by the next enrolled patient. Whether treatment allocation was performed by an independent person is not described in both studies.

Were the groups similar at baseline regarding the most important prognostic indicators?

The baseline systolic BP was approximately 3 mmHg higher in the intervention group in both studies. The results in both studies were presented without adjusting for this baseline difference. All other baseline variables were comparable between groups in both studies.

Were the patients, care providers and outcome assessor(s) blinded to the intervention?

None of the patients in the Logtenberg *et al.* study were informed about the treatment in the other study group. A questionnaire at the end of the study showed that blinding was successful. The patients in the Schein *et al.* study were not blinded to the intervention. Blinding of the care providers was not possible in both studies. All patients were seen and the outcomes were measured by the same investigators.

Were co-interventions avoided or similar? Was the compliance acceptable in all groups?

Patients in both studies were instructed to continue usual care, including pharmacological treatment, diet and physical exercise. Logtenberg *et al.* did not describe any change in these parameters. One patient had to change medication in the Schein *et al.* study. A total of 94% of the recommended daily breathing sessions were performed by all patients in the Logtenberg *et al.* study, compared with 75% reported by Schein *et al.* Although the compliance rate was very high in the Logtenberg *et al.* study, only 60% of the patients achieved the target range of less than

ten breaths per minute (measured at the end of the daily sessions). In the Schein *et al.* study, 60% of the total session time was spent in the 'therapeutic breathing zone'.

Was the withdrawal/drop-out rate described and acceptable? Was the timing of the outcome assessment in all groups similar?

No patients were lost to follow-up in the Logtenberg *et al.* study. Five of the 38 patients in the intervention group of the Schein *et al.* study dropped out after 4 weeks. One patient complained of mild dizziness, one had to change medication and another three patients did not use the device at all. BP was measured at the end of the study in both investigations.

Did the analysis include an intention-to-treat analysis?

Authors of both studies claim to have performed an intention-to-treat analysis. Five patients dropped out from the intervention group in the Schein *et al.* study. The authors mentioned that no follow-up BP measurements were performed for four patients and that baseline values were used instead. This method is considered to be conservative by the authors. As systolic BP increased in the control group, use of baseline BP for the four patients results in a between-group-difference in favor of the intervention group. Therefore, use of the baseline BP values can not be seen as conservative.

Studies fulfilling six or more of the 11 quality criteria are considered to be of high quality. All studies scoring less than six of the criteria are rated as low quality [15]. The study by Logtenberg *et al.* scored positive for eight criteria, compared with five for the Schein *et al.* study. The study by Logtenberg *et al.* was superior with respect to the method of randomization, blinding of the patients and the intention-to-treat analysis. These differences in study design could be a cause of the discrepancies in results between both studies. There are two other aspects that merit highlighting. First, in both studies, systolic BP significantly decreased in the intervention group. However, the study by Schein *et al.* used usual care as a control group, whereas the study by Logtenberg *et al.* used an active control (listening to music with a portable CD player). With the use of such a control group, they intended to specifically study the effects of slow breathing [13,14]. A previously published editorial emphasized that an independent double-blind study design with a proper control group

will be necessary to answer the question of whether device-guided breathing has any effect on BP [16]. Second, the Logtenberg *et al.* study has an important limitation with respect to the wide 95% CI (-2.3–11.7) of the change of systolic BP between groups. The study was powered to detect an absolute reduction of 10 mmHg in systolic BP, and the upper limit of the confidence interval exceeded the boundary of 10 mmHg (in the direction in favor of the control group).

“The results of the two trials in patients with T2DM are conflicting...”

At present, only one study with an acceptable study design has demonstrated a significant decrease in systolic BP in nondiabetic patients [5]. The results of the two trials in patients with T2DM are conflicting; however,

when taking the methodological quality of the studies into account, we have to conclude that there is no basis for this treatment modality in diabetic patients. An independent double-blind randomized trial needs to be performed in order to make a definite and more precise conclusion regarding efficacy. Until then, we recommend not to use device-guided breathing for the treatment of hypertension in patients with T2DM.

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