Device-Guided Breathing for Hypertension: a Summary Evidence Review

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Abstract

Persistently raised blood pressure is one of the major risk factors for diseases such as myocardial infarction and stroke. Uncontrolled hypertension is also associated with high rates of mortality, particularly in middle and high-income countries. Lifestyle factors such as poor diet, obesity, physical inactivity and smoking are all thought to contribute to the development of hypertension. As a result, the management of hypertension should begin with modifying these lifestyle factors. Beyond this, drug interventions are used as the predominant form of management. However, adherence to medications can be highly variable, medication side effects are common, and may require regular monitoring or, in some individuals may be ineffective. Therefore, additional non-pharmacologic interventions that lower blood pressure may be advantageous when combined with lifestyle modifications. Such interventions may

include relaxation therapies such as slow breathing exercises, which can be initiated by means of specific devices. The technique of device-guided breathing (DGB) has been considered by guideline developers in the management of hypertension. One specific device, the Resperate, has received US FDA and UK NHS approval over the last few years. In this review, we summarise the evidence base on efficacy and find that although some clinical trials exist that demonstrate a BP-lowering effect, others do not. There is currently insufficient evidence from pooled data to recommend the routine use of device-guided breathing in hypertensive patients.

Keywords

Blood pressure

Hypertension

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Introduction

According to the World Health Organization, approximately 22 % of adults aged 18 and over have raised blood pressure. Hypertension is one of the major risk factors for mortality, with the highest risk in middle and high-income countries worldwide [1]. Hypertension is also associated with multiple morbidity, particularly heart failure, myocardial infarction and stroke and lowering blood pressure is associated with improved outcomes [2].

Lifestyle factors such as poor diet, obesity, physical inactivity and smoking are associated with the development of hypertension and subsequent ill health [3, 4•]. At diagnosis, patients with stage 1

hypertension (defined as clinic readings of 140/90 mmHg or higher and daytime average ambulatory or home blood pressure monitoring of 135/85 mmHg or higher), are encouraged to incorporate lifestyle changes as the first stage of management [2]. This may include modifying alcohol intake, reducing salt consumption, smoking cessation, weight loss, dietary changes and increased physical activity. Those patients who fail to respond, or have additional risk factors, are likely to be commenced on pharmacotherapies, which currently remain the mainstay of hypertension control and risk management [2]. However, adherence to anti-hypertensive drug medication is highly variable ranging from 40 to 90 % depending on the population [5]. Poor compliance is also associated with negative outcomes [6–8]. Therefore, modifying behaviour and sustaining lifestyle changes are seen as essential in hypertension management [9, 10]. As part of the lifestyle management of hypertension, the UK National Institute for Clinical and Health Excellence (NICE) found some evidence that relaxation therapies may reduce blood pressure [11]. These could include stress management, meditation and biofeedback approaches. However, a Cochrane systematic review found only weak evidence of a causal relationship between relaxation therapies and long-term improvements in blood pressure [12]. Therefore, current UK guidelines do not currently recommend the widespread use of relaxation-based therapies [2, 11].

Hypertension and Slow Breathing

Although primary hypertension has a multifactorial aetiology, persistently raised blood pressure is associated with abnormal autonomic, increased sympathetic and decreased parasympathetic, activity. Such activity leads to increased arterial and venous constriction as well as increased vascular resistance

[13, 14]. Building on this understanding, it has been postulated that forced biofeedback may act as a way to reduce blood pressure through effects on pulmonary, cardiac and arterial stretch receptors [15]. Such activities may include changes in breathing rates, and in particular slow breathing [16•]. The act of slow deep breathing activates cardiac and pulmonary stretch receptors, decreases sympathetic activity and increases parasympathetic activity and vagal tone, with concomitant changes in heart rates and blood pressure [16•, 17]. The resultant acute reductions in blood pressure are thought to augment the baroreflex sensitivity and reset the deranged autonomic balance in hypertensive patients [18]. Therefore, it has been hypothesised that regular systemic instructions to voluntarily breath slowly could lead to chronic reductions in blood pressure thus providing an additional management option for hypertensive patients [16]. Achieving slow deep breathing is an integral part of meditation and yoga, two practices that have received some interest with equivocal results as complementary therapies in the treatment of hypertension [19, 20]. Therefore, preprogrammed clinical devices may deliver more controlled breathing instructions that may impact positively on reducing blood pressure [21].

In 2002, the FDA approved the Resperate (InterCure Ltd, Israel) device as an adjunct anti-hypertensive treatment approach that guides home users to alter their breathing rate in response to instructed signals [21, 22, 23•]. The device consists of a control box, headphones and a respiratory rate monitor attached as a sensor belt around the user's chest (Fig. 1). The user is instructed to alter their breathing rate, aiming for 10 breaths per minute, in response to a melody played to them via the attached headphones. Users are asked to use the device for at least 40 min per week, with each session lasting at least 10 min [23•].

Fig. 1

The Resperate (InterCure Ltd, Israel) device is an adjunct anti-hypertensive treatment approach that guides home users to alter their breathing rate in response to instructed signals (reproduced with permission from MedScape)

Evidence Base for Device-Guided Breathing in Hypertension

Device-guided breathing (DGB) units, such as the Resperate, are available to the public and are marketed as an effective non-pharmacological adjunct treatment for high blood pressure [23•].

The Resperate device itself has a Class IIA recommendation from the American Heart Association (AHA) for this purpose [24]. In 2012, the UK NHS Business Authority approved it for addition onto a new list entitled 'Devices for the adjunctive treatment of hypertension' available to patients via an NHS prescription from their doctor [25].

Two of the authors (KRM and DN) published a systematic review and meta-analysis of randomised controlled trials examining the effects of DGB on blood pressure changes [26••]. The review included eight randomised controlled trials (RCTs) including data from 494 adult patients. Included trials came from three countries (Israel, the Netherlands and the USA) and all studies included patients with existing hypertension. The Resperate device was used as the active intervention in each of the studies although the control intervention varied between included studies. In six of the studies, the authors attempted to control for the intervention device using a device that plays music only (with no instructions on altering breathing rate). In one of the remaining studies, the authors used a standard BP monitoring unit and in the other remaining study, the authors used 'standard care' as the comparator.

The quality of the included studies was highly variable with an overall moderate to high risk of bias. Results were therefore interpreted with caution. In the office setting, DGB resulted in a significant decrease in systolic blood pressure (SBP) of 3.06 mmHg (95 % CI −4.68 to −1.43 $P = 0.0002$) compared to control interventions. Diastolic blood pressure (DBP) was also significantly decreased by 2.35 mmHg (95 % CI −3.47 to −1.22 $P = 0.0001$) in this setting. Four included studies examined the impact of the device using home BP measurements and meta-analysis of these four studies revealed a decrease in SBP of 2.46 (95 % CI −4.74 to −0.18 $P = 0.03$) and a decrease in DBP of 2.22 mmHg (95 % CI −3.74 to −0.66 $P = 0.005$). No difference was found for changes in heart rate.

A key requirement of the device's efficacy is that the user slows their breathing to 10 breaths/min [23•]. However, many of the included studies provided insufficient information to determine whether this was achieved in the clinical trials. Adherence to the device was also inconsistently reported within the included studies, an unfortunate omission when considering the potential real world use of this device. In addition, the majority of trials provided intervention data for no longer than 8 weeks.

Device-guided breathing use did not alter any changes in quality of life measures as assessed using patient filled out questionnaires, such as the 36-item Short Form Health Survey and the WHO five-item Wellbeing Index. One study included within the review reported a patient feeling dizzy after using the DGB intervention, although there were no reported adverse events in the remaining studies.

As many of the studies were sponsored by, or involved, the manufacturer of the device, a sensitivity analysis was carried out, excluding these studies. Meta-analysis of the remaining three studies found there to be no significant effect on SBP or DBP, although heterogeneity was higher. Given the small

nature and variable quality of the included studies, the review concluded that efficacy and effectiveness needed to be demonstrated from further high quality research before DGB could be part of routine clinical practice or policy [26••].

Since that original systematic review, two randomised controlled trials and one individual patient meta-analysis have been published, relevant to this topic [27, 28•, 29••]. One of these new clinical trials studies was a proof-of-concept study and examined whether Resperate could effectively reduce BP in hypertensive patients (on medication) and with either type 1 or type 2 diabetes. Thirty two patients were recruited into the study and after 8 weeks significant reductions were demonstrated in 24 h SBP with DGB (126.1 ± 3.0 vs. 123.2 ± 2.7 mmHg, $P = 0.01$) that were not seen in the control arm receiving only 'usual care' which included the non-pharmacological treatment in the form of lifestyle advice and in some cases pharmacological management. However, this effect was not reproduced for several of the other planned outcomes including daytime SBP, DBP and mean arterial pressure [27].

The second trial examined the effect of Resperate in lowering blood pressure in hypertensive patients with type 2 diabetes [28•]. Forty-eight patients were randomised in the study. The study was independent of any connection to the manufacturer of the device and was generally of higher quality than previous ones, notably being double blind. The study also used a sham device in the control arm in which participants had an identical looking device but guided users to a breathing frequency of approximately 14 breaths/min (rather than 10 breaths/min as advocated by the Resperate). Adherence (measured by mean breathing frequency) was achieved in both arms; 5.7 breaths/min in the intervention group and 14.3 breaths/min in the control group ($P < .001$). The authors found no

significant changes in systolic and diastolic blood pressure between the two arms of the study. However, the study was also limited to an 8-week intervention period. Of particular note was the reporting of three adverse events, all of which occurred in the intervention arm. The study recorded that one patient died of respiratory failure due to underlying heart failure, one patient reported atypical chest pain while another shortness of breath. Both latter patients refused to use the Resperate device any longer [28•].

A more recent individual patient data (IPD) meta-analysis focused on high quality trials with active control [29••]. Strict inclusion criteria resulted in five RCTs being methodologically acceptable for inclusion and subsequent meta-analysis. However, the final analysis was limited to only three trials, all from an independent group based in the Netherlands (some of whom were also co-authors of the IPD). The authors reported that no data was provided from the authors of the other included trials as well as from the manufacturer of the device, despite numerous requests for this information. The meta-analysis of available data demonstrated that DGB did not offer any beneficial treatment effect for either systolic or diastolic blood pressure. The authors also reiterated the finding that one of the included trials reported three patients with adverse events, all in the Resperate arm (as described above), and concluded that current best evidence does not support the routine use of this device [29••].

Current Recommendations for Device-Guided Breathing Devices

In 2012, the UK British Hypertension Society issued a statement in response to a number of queries about the availability of the Resperate device via NHS prescription [36]. The statement, based on the recently published systematic review and meta-analysis, advised that there was insufficient evidence

for this equipment to be recommended in routine clinical practice. In 2013, NICE carried out an NHS Evidence update for Hypertension, emphasising that DGB was not currently recommended for routine use in patients with hypertension [37].

A scientific statement from the American Heart Association (AHA) evaluated evidence for alternative approaches to lowering blood pressure [38•]. Within this statement was a specific review of the evidence for DGB in lowering BP in hypertensive patients. The writing group afforded DGB a Class IIA, Level of Evidence B recommendation for BP-lowering efficacy. Although limited populations had been evaluated, in the opinion of the writing group, the device provided significant benefits over risks and, although more studies may be needed, it was reasonable to use the device in practice. However, the statement drew criticism from some of the authors of the IPD who disagreed with the recommendation and advocated a reduction in the level of recommendation [29••]. Members of the writing group responded to this criticism stating that 'the modest potential benefits derived from device-guided slow breathing should not be entirely discounted' [39]. A more recent follow on report from some of the authors of the AHA statement, also provides guidance on when and how to implement these methods in clinical practice, including device-guided breathing [40].

Conclusion

There is a growing call to emphasise treating high blood pressure with lifestyle (non-drug) changes. These include changes in diet, physical inactivity levels, alcohol and relaxation therapies [2]. One current non-drug intervention, approved by the FDA, is a device that guides users to slow their

breathing rate and, through regular sessions of use, is being marketed as an adjunct to manage hypertension [23•].

Despite regulatory approval and numerous clinical trials, the evidence-base for device-guided breathing as a treatment for hypertension is inconclusive. Efficacy data from existing studies are limited by small sizes and, in some cases, poor methodological quality; concerns with safety; [25] and a lack of a large, well designed and conducted, independent randomised controlled trial. Currently, based on systematically collected, appraised and analysed data, there is insufficient evidence to recommend the routine use of device-guided breathing in hypertensive patients [26••, 29••].

Compliance with Ethical Standards

Conflict of Interest

Drs. Mahtani, Beinortas, Bauza, and Nunan declare no conflicts of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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