Journal of Human Hypertension (2001) 15, 271–278

www.nature.com/jhh

ORIGINAL ARTICLE

Treating hypertension with a device that slows and regularises breathing: a randomised, double-blind controlled study

MH Schein[1], B Gavish[2], M Herz[3], D Rosner-Kahana[3], P Naveh[1], B Knishkowy[1], E Zlotnikov[3], N Ben-Zvi[3] and RN Melmed[4]

[1]*Family Medicine Unit, Hadassah University Hospital,* [2]*InterCure, Neve Ilan,* [3]*Department of Family Medicine, Tel Aviv University and Kupat Holim Clalit,* [4]*Unit of Behavioural Medicine in Internal Medicine, Department of Medicine, Hadassah University Hospital, Israel*

Objective: **To examine the efficacy of a new device, which slows and regularises breathing, as a non-pharmacological treatment of hypertension and thus to evaluate the contribution of breathing modulation in the blood pressure (BP) reduction.**

Design and setting: **Randomised, double-blind controlled study, carried out in three urban family practice clinics in Israel.**

Patients: **Sixty-five male and female hypertensives, either receiving antihypertensive drug therapy or unmedicated. Four patients dropped out at the beginning of the study.**

Intervention: **Self treatment at home, 10 minutes daily for 8 consecutive weeks, using either the device (n = 32), which guides the user towards slow and regular breathing using musical sound patterns, or a Walkman, with which patients listened to quiet music (n = 29). Medication was unchanged 2 months prior to and during the study period.**

Main outcome measures: **Systolic BP, diastolic BP and mean arterial pressure (MAP) changes from baseline.**

Results: **BP reduction in the device group was significantly greater than a predetermined 'clinically meaningful threshold' of 10.0, 5.0 and 6.7 mm Hg for the systolic BP, diastolic BP and MAP respectively (P = 0.035, P = 0.0002 and P = 0.001). Treatment with the device reduced systolic BP, diastolic BP and MAP by 15.2, 10.0 and 11.7 mm Hg respectively, as compared to 11.3, 5.6 and 7.5 mm Hg (P = 0.14, P = 0.008, P = 0.03) with the Walkman. Six months after treatment had stopped, diastolic BP reduction in the device group remained greater than the 'threshold' (P < 0.02) and also greater than in the Walkman group (P = 0.001).**

Conclusions: **The device was found to be efficacious in reducing high BP during 2 months of self-treatment by patients at home. Breathing pattern modification appears to be an important component in this reduction.**

Journal of Human Hypertension (2001) **15,** 271–278

Keywords: high blood pressure; non-pharmacological therapy; device; breathing exercises

Introduction

Hypertension has been well documented as a major risk factor for cardiovascular morbidity and mortality.[1] The side effects and cost of antihypertensive drugs have led to a consensus about the need for effective non-pharmacological treatment alone or adjunctive to drug therapy.[1]

Although not specifically emphasised, slow and regular breathing plays a prominent role in behavioural methods such as yoga, meditation and biofeedback and these methods have had some success in treating high blood pressure (BP).[2–10] Past research suggests that a slow and regular breathing pattern has a number of beneficial effects in the reflex control of the cardiovascular system.[11,12] However, the specific role played by breathing exercises in the sustained reduction of high BP has not been evaluated by well-controlled studies.

We hypothesised that the routine practice of a slow and regular breathing pattern may reduce high BP. The hypothesis was tested using a new device called BIM (Breathe with Interactive Music). The BIM guides the user towards slow and regular breathing by creating a musical pattern temporally related to the breathing movements monitored by a sensor.[13]

The two principal objectives of this study were to examine the efficacy of the BIM device in reducing

Correspondence: Dr Moshe Schein, Family Medicine Unit, Hadassah University Hospital, PO Box 12000, Jerusalem 91120, Israel. E-mail:beny@intercure.co.il (via Dr B Gavish)
Request for reprints: Dr Benjamin Gavish, InterCure, Communication Park, Neve Ilan, 90850, Israel
Received 7 June 2000; revised 23 July 2000; accepted 8 August 2000

high BP and to evaluate the contribution of breathing modulation in the BP reduction. We employed a double-blind, randomised study design with an active control group using an alternative device (Walkman).

Patients and methods

Patients

This study was approved by the research ethics committee of the Hadassah University Hospital and was carried out at three independent urban family practice clinic sites (I, II and III). The study was first conducted at site I and then repeated at sites II and III for additional verification, in view of the outcome favouring our hypotheses which was shown in the site I study.

Inclusion criteria were patients aged 25–75 years with elevated BP, unmedicated or constantly medicated with the same drugs and at the same doses for at least 2 months prior to the study. Hypertension was defined in site I as average systolic BP $\geqslant$140 mm Hg and/or a diastolic BP $\geqslant$90 mm Hg during the year prior to the study and at the enrolment visit. In sites II and III, patients eligible for inclusion had a BP $\geqslant$140/90 mm Hg at two visits, several days apart, enrolment taking place during the second visit. In site I BP measurements were registered during the year prior to the study. Exclusion criteria were active ischaemic heart disease, chronic atrial fibrillation, congestive heart failure, stroke, diabetes mellitus, chronic renal failure, asthma, chronic respiratory disease, other major organ failure, panic disorder, major psychiatric diagnoses, pregnancy, a body mass index (BMI) $>$35 (in sites II and III) and an inability to operate a portable tape.

Sixty-five subjects were enrolled in the study (n = 28, 24 and 13 for sites I, II and III, respectively) following a medical chart review of patients registered in the three family practice clinics. The patients were told that in order to measure the efficacy of the device in reducing hypertension, treatment would consist of listening at home in a quiet room to special music produced by one of two devices, for 10 min each day during an 8-week period. No mention was made of breathing exercises. Written informed consent was obtained.

Study procedures

The BIM device (prototypes manufactured by InterCure Ltd, Neve Ilan, Israel) used in the treatment group, consists of a belt-type respiration-movement sensor mounted on the upper abdomen or chest, a computerised control unit and headphones. Based on the analysed monitored breathing pattern, the device composes in real-time music-like sound patterns with a temporal structure similar to the actual breathing pattern but with prolonged 'expiration' (in the sound pattern). The breathing pattern modification occurs as the user voluntarily follows the sound pattern with his/her breathing movements.[13] This process continues until it reaches a steady state at the lowest breathing rate convenient to the user. A Walkman was used as an active control, playing a 10-min recorded cassette of quiet synthesised music similar to that of the BIM, however with a non-identifiable rhythm. The justification for the use of a Walkman as a control will be related to in the Discussion section.

The BP was measured in a sitting position, after the patient had rested for 5 min. All readings were taken with an appropriately sized cuff placed on the right upper arm parallel to the trunk. The doctors were trained to use phase I Korotkoff sounds to define the systolic BP and the disappearance of sound (phase 5) as the measurement of the diastolic BP. A single BP measurement was determined as follows: in site I—two readings using two different sphygmomanometers. The first with a standard mercury sphygmomanometer and the second with an aneroid sphygmomanometer. In sites II and III—three to five readings with a standard mercury sphygmomanometer until two consecutive BP readings did not differ by more than 10%. The use of two different BP monitors in site I was done in an attempt to check dependence of measurements on the device type (found to be insignificant).

The patients' compliance with treatment was checked by the personal diary they had been asked to sign each day, confirming that they had carried out the treatment. More information was obtained for the BIM treatment from data stored in data loggers installed in the 18 devices supplied to sites II and III only. This information included the number of sessions and minutes of use as well as the average breathing rate at the end of each session.

Study design and protocol

The study was randomised, double blind with parallel design and active control in order to examine the efficacy of the BIM device in reducing high BP and evaluating the contribution of breathing modulation in the BP reduction. Efficacy was defined as the ability of the device to reduce high BP by more than at least one of the following 'clinically meaningful thresholds': 10, 5, and 6.7 mm Hg for systolic BP, diastolic BP and mean arterial pressure (MAP), respectively. These figures represent half a stage in the JNC-6 classification of hypertension for adults age 18 years and older.[1] This choice is justified since a reduction of this magnitude is likely to benefit the patient in terms of lower mortality and fewer serious vascular events.[14,15] The contribution of breathing modulation in the possible BP reduction was examined by comparing the BP reduction in the BIM and Walkman devices.

Study stages

The participants visited their clinic for BP measurements while receiving self-treatment at home (Figure 1). Enrolment took place at the last baseline visit (one visit at site I and two visits at sites II and III). At enrolment, inclusion and exclusion criteria were examined. The patient's medical history including medication list was recorded and a physical examination performed. The patients were requested to sign a diary each day confirming that they had indeed carried out the treatment.

Randomisation was carried out by a third party on small groups of enrolled patients according to the following procedure: a list of two or more patients was sorted with preferences for MAP, age and gender in that order, creating a list in which consecutive patients are best matched. After dividing the list into pairs (1st and 2nd, 3rd and 4th, etc), the patients in each pair were randomly assigned into the BIM or Walkman groups, using a table of random numbers.

Devices were delivered and maintained by a technician at the patient's home. The technician instructed the patients to treat themselves by listening to the device music (while performing breathing exercises, in the BIM group) 10 min daily for 8 weeks. The instruction for the self-treatment, using the devices, was similar in both groups and lasted about 30–45 min. The technician was available via a mobile phone to help the patients solve technical problems. The technician also collected the personal diary forms at intervals during the study period.

The treatment took place at home, during the afternoon or evening, with the patient seated comfortably in a quiet room and avoiding any disturbances, for example, use of telephone, television or talking to other persons. No change was made in the antihypertensive medication during the whole study period.

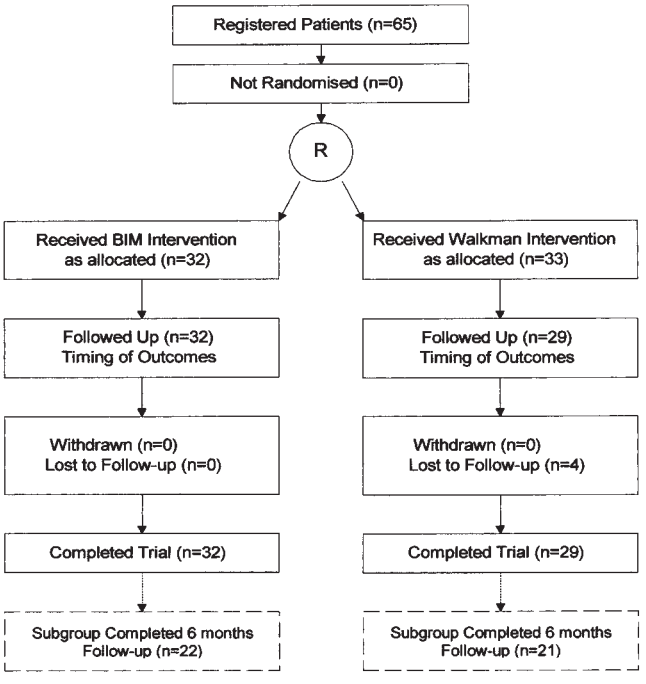

Figure 1 Progress through the various stages of the study.

Double blinding was achieved by both the doctors and the patients being unaware of group assignment and the technician being blinded to the patient's BP measurements at the clinic. In order to minimise accidental unmasking, patients were requested not to talk about the specific device with the doctor and other persons who may be participating in the study.

After enrolment, the study participants were invited at a similar hour at weekly intervals to the Family Practice Clinic where the same doctor measured their BP and heart rate. At the end of 8 weeks of treatment the subjects were questioned for adverse reactions, and comments not reported during the study were noted. In addition, the doctor performed a physical examination and checked concomitant medication. After this final visit the technician collected the devices.

Although not part of the original study protocol, all patients were asked to return for a follow-up visit 6 months after termination of treatment. Only 43 agreed.

The rules for a patient's withdrawal from the study were firstly a change in the medical condition that would not allow the patient's continued participation according to the protocol. Secondly, nonadherence to the protocol, mainly failure to visit the clinic for BP measurements.

Data analysis

BP level per visit was calculated from the sequence of consecutive measurements by averaging the readings. For study I (four BP readings) we have calculated the deviation of each reading from the average BP value measured for a specific patient and visit. This deviation created a Gaussian distribution around zero with a standard deviation (s.d.) = 4.5 and 3.3 mm Hg for the systolic and diastolic BP, respectively. We have excluded 5% of the systolic or diastolic BP data (93/1908 measurements) that deviated by two or more standard deviations from the average value measured at each visit, but not more than a single data measurement per visit. This procedure is justified since it was applied as an objective tool to reject erroneous measurements corresponding to large changes in BP observed in a sequence of BP readings. Such errors were observed when patients moved or thought and reported stressful situations during BP measurements.

In studies II and III, three to five BP readings were measured, stopping when readings did not differ by more than 10%. BP level per visit was calculated by averaging the data of all consecutive readings that were closer than 10%, ie the difference between the two consecutive measurements divided by their average value was less than 0.1, for either systolic or diastolic consecutive measurements.

Baseline BP level was defined as the average BP measurements at one (site I) or two visits (sites II and III) during enrolment. The primary study outcomes for an individual patient were changes in the systolic BP, diastolic BP and MAP from baseline to 'end value', where the latter was calculated as the average of the BP level measured during the last 5 weeks of treatment. The justification is described in the statistical analysis section. The same analysis was applied for calculating changes in the heart rate.

Statistical analysis

Estimation of sample size was made at first for site I, using the data of Patel and North,[6] whose study had some similarity to our design, since treatments included breathing exercises compared to general relaxation. Standardised detectable difference ($\Delta\mu/\sigma$) for the systolic BP was found to be 0.78 (with pooled standard deviation), which provides a minimal group size of $n = 13$ for comparing the treatments with a significance level of $P < 0.05$ with 80% power of test. Using the results obtained at site I we obtained a standardised detectable difference of 0.67, which gives an n equals 18 for sites 2 and 3 under the same requirements.

Analysis was performed using the following tests: justification of data pooling from different sites was tested by comparison by site of baseline characteristics and study outcomes for each group using ANOVA for continuous variables and chi-square for categorical variables. For comparison of baseline characteristics between the treatment groups *t*-test for continuous variables and Fischer's exact test for categorical variables. The justification for selecting a time period for defining 'end value' of BP change, ie the plateau region shown in Figure 2, was done by grouping data into the five 2-week segments shown in Figure 2, as 'prior treatment' and Quarters 1 to 4, covering the 8-week treatment period. In that way each time segment included patients who had outcomes. We then performed repeated measure analysis with ANOVA for evaluating the variance of MAP for all patients and for MAP change of each treatment group during the last *n* time segments (for example, for $n = 2$ we compared all data measured during Quarters 2 to 4). The efficacy of the BIM device in reducing high BP was tested using a one-sample *t*-test for each outcome, ie systolic BP, diastolic BP and MAP changes. The comparison of treatment effects on outcomes was tested using a linear regression model that included as covariates, baseline BP value, age and the interaction of these covariates with the type of treatment. The possible effect of the categorical variables gender and medication status on outcomes was evaluated for each treatment group using the *t*-test. All the tests were two-tailed.

Results

Baseline characteristics of the 65 enrolled subjects in the study are presented in Table 1. Four patients, all from the control group, were lost to follow-up at the treatment period and thus had no outcomes. Three of them had one or fewer visits, explained by the lack of time and refusal to collaborate and an additional patient stopped after three visits since she travelled abroad. The remaining 61 subjects comprised the cohort of 'compliant patients' (Figure 1), which is identical with all intent-to-treat patients having outcome measures. The BP changes in response to treatment are shown in Table 2.

The BP reduction in the BIM group was significantly greater than a predetermined 'clinically meaningful threshold' of 10.0, 5.0 and 6.7 mm Hg for the systolic BP, diastolic BP and MAP respectively ($P = 0.035$, $P = 0.0002$ and $P = 0.001$). No

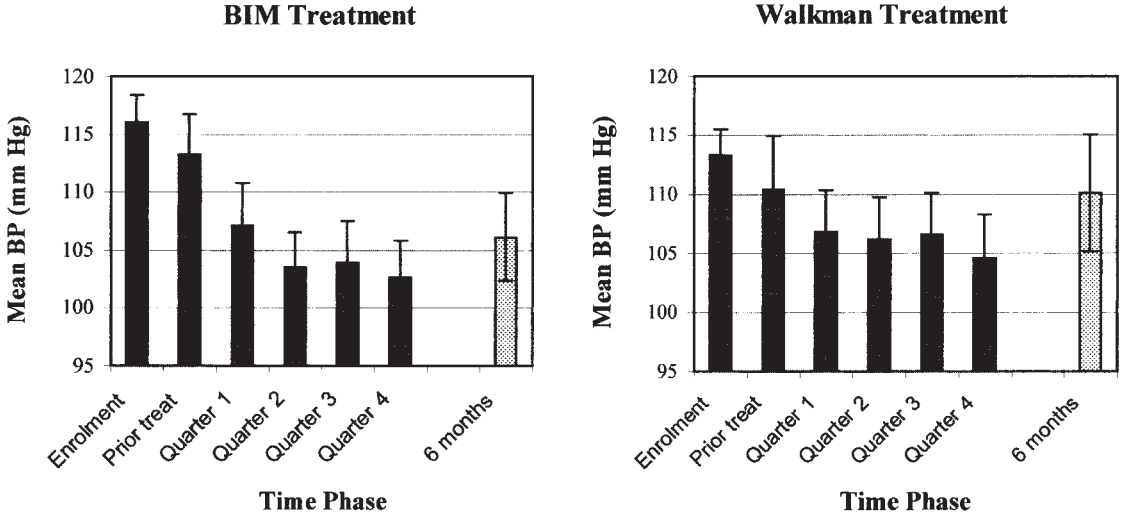

Figure 2 Variations of MAP (with s.e.) during the study (dark grey) for all patients ($n = 61$), and 6 months after treatment ended (light grey) for a subgroup of patients ($n = 43$), who were willing to visit the clinic. The bar marked by 'prior treat' refers to 10 days prior to delivery of devices and the 'Quarter 1' to 'Quarter 4' refer to 2-week intervals that include the treatment period.

Table 1 Characteristics of study population on enrolment

	BIM treatment (n = 32)	*Walkman treatment (n = 33)*	*P-value*
Age (years)	57.8 ± 9.4	56.5 ± 8.0	0.57
% Males	56%	39%	0.22
Body mass index	28.9 ± 3.7	28.9 ± 5.2	0.99
% Medicated	91%	76%	0.19
Systolic BP (mm Hg)	156.6 ± 14.0	154.7 ± 8.5	0.50
Diastolic BP (mm Hg)	96.7 ± 8.9	93.4 ± 7.1	0.10
MAP (mm Hg)	116.7 ± 9.1	113.8 ± 6.1	0.14
Heart rate (bpm)	72.6 ± 12.4	71.7 ± 8.6	0.73

Values are average ± s.d. and %. The *P*-value was obtained by *t*-test for continuous variables and Fischer's exact test for categorical variables.

similar significant BP reduction was observed in the Walkman group. In the BIM group 25/32 patients (78%) had a MAP reduction greater than threshold, whereas 17/29 (59%) in the Walkman group had a similar reduction.

The reduction of diastolic BP and MAP changes was significantly greater in the BIM group compared to the Walkman group ($P = 0.008$ and 0.03). The systolic BP changes displayed a similar trend but did not reach statistical significance. The corresponding heart rate changes were not significant: 2.0 ± 9.6 for the BIM group and 1.7 ± 7.6 for the Walkman group.

There was no association of the outcomes of either group with gender ($P > 0.15$). The number of unmedicated patients was too small to test a possible association of outcomes with the medication status. No adverse reactions were reported during the study.

The main reduction of BP in both groups was achieved within the first month of treatment with the BP reaching a plateau during the last 5 weeks (Figure 2). This observation is confirmed by finding no significant difference between MAP of all patients measured at Quarters 2, 3 and 4 ($P > 0.8$, for comparison with ANOVA). A drop in BP in both groups occurred between enrolment and delivery of the devices which marked the start of treatment (2.8 and 2.9 mm Hg for the MAP in the BIM and Walkman groups, respectively, $P > 0.9$).

Compliance of patients in the BIM group could be evaluated from data obtained from 14 of the data loggers in the 18 BIM devices used in sites II and III. Due to technical problems we were unable to download files stored in four BIM devices. Data showed that, on average, each patients used the BIM for 43 sessions (out of 56 requested) and for 7.3 min (out of 10 min requested). The average end-breathing rate in a treatment session was 8.4 per min. This value is lower than the normal breathing rate, which is usually in the range of 12 to 20 per min.

Forty-three out of the 61 patients complied with the request to re-examine their BP 6 months after the treatment with the BIM or Walkman had been terminated and devices returned. The baseline characteristics of patients from each treatment group, who came for a 6-months follow-up visit were compared. No significant differences were found ($P > 0.05$). During this period hypertension medication had been changed (reduced) in only one patient included in the BIM group. The results (Table 3) demonstrate that at 6-months follow-up the diastolic BP reduction was still significantly greater than the threshold of 5 mm Hg ($P < 0.02$), and the decrease in the BP was significantly greater in the BIM group as compared to the Walkman group ($P = 0.04$ and $P = 0.001$ for systolic and diastolic BP changes, respectively).

Discussion

Our basic study hypothesis was that routine exercise, during which breathing is slowed down, can reduce high BP. It should be emphasised that no assumption was made that the BP effects are related to a sustained change in the respiration pattern. In the study reported here, guided breathing exercises

Table 2 Blood pressure response to treatment and its significance concerning the treatment efficacy and the role of breathing in the BP reduction[a]

	BIM treatment (n = 32)		*Walkman treatment (n = 29)*		*95% CI of difference*	*P-value for group comparison*
	Change	*P-value for 'efficacy'*	*Change*	*P-value for 'efficacy'*		
Systolic BP (mm Hg)	−15.2 ± 13.4	0.035	−11.3 ± 12.8	0.58	−2.8 to 10.6	0.14
Diastolic BP (mm Hg)	−10.0 ± 6.5	0.0002	−5.6 ± 6.2	0.59	1.1 to 7.6	0.008
MAP (mm Hg)	−11.7 ± 7.8	0.001	−7.5 ± 7.9	0.57	0.2 to 8.2	0.03
Heart rate (bpm)	2.0 ± 9.6		1.7 ± 7.6		−4.9 to 4.1	0.87

Values in columns 2 and 4 are average ± s.d. in mm Hg. Column 6 corresponds to the 95% confidence interval for the difference between BP changes observed in the two treatments. The *P*-values in columns 3 and 5 were obtained by one-sample *t*-test. The *P*-values in column 7 are covariate-adjusted for age and baseline BP and were obtained by using the linear regression model.
[a]Pooling of BP changes among the three study sites was justified, since there were no statistically significant differences ($P > 0.05$) in changes of systolic BP, diastolic BP, MAP and heart rate between the first site and the second and third sites combined, in response to treatment with either the BIM or the Walkman.

Table 3 Blood pressure changes from baseline at the end of treatment and 6 months later after treatment ended in a subgroup of patients who visited the clinic for re-examination

	BIM treatment (n = 22)	*Walkman treatment (n = 21)*	*95% CI of difference*	*P-value*
	Change in mm Hg	*Change in mm Hg*		
End of treatment				
Systolic BP	−16.8 ± 12.9	−11.7 ± 13.5	−3.1 to 13.2	0.18
Diastolic BP	−11.5 ± 6.2	−5.4 ± 6.8	2.0 to 10.1	0.002
6 months after treatment ended				
Systolic BP	−9.7 ± 11.4	−4.1 ± 17.5	−3.5 to 14.6	0.04
Diastolic BP	−9.0 ± 7.3	−1.2 ± 9.2	2.7 to 12.9	0.001

Values in columns 2 and 3 are average ± s.d. in mm Hg. Column 4 corresponds to the 95% confidence interval for the difference between BP changes observed in the two treatments. The *P*-value in column 5 is covariate-adjusted for age and baseline BP and was obtained using the linear regression model.

performed with the BIM device at home for about 10 min daily, were associated with a significant reduction of BP in hypertensive patients by a clinically meaningful value of 15/10 mm Hg for systolic and diastolic BP, respectively. This is indeed a substantial BP reduction especially when compared to other accepted non-pharmacological therapies, for example, aerobic-exercise training[16] and reduced salt dietary intake[17] which reduced high BP by 6/5 and 6/2 mm Hg, respectively.

Both the BIM and the Walkman groups listened to music. However, during the intervention respiration was actively modulated only in the BIM group. The greater effect in this group suggests that modulation of breathing is the active component. The lack of identification of an active element in the so-called 'behavioural treatments' of hypertension adds to the controversy concerning their efficacy. No previous attempt has been made to evaluate the possible role specifically played by the breathing pattern in reduction of high BP using a double-blind, randomised study design.

In most studies the control group either did not do anything or performed some other activity such as relaxation exercises. The choice of Walkman as an active control in our study satisfied the criteria of a 'good control'.[18,19] Like the BIM, it is a handheld device and its use entails listening to music. Both groups underwent a short period of technical training and treatment was carried out under similar environmental conditions. The Walkman was different from the BIM in that its use does not entail active breathing exercise, thus allowing us to isolate the effect under study. The effect of the Walkman has potential benefits, since it has been demonstrated that quiet music can elicit a cardiovascular response in the direction opposite to that caused by mental stress.[20,21]

The BP reduction observed in the Walkman group could be ascribed to the so-called 'relaxation response'[22] and is consistent with the view in the literature of the physiological response to quiet music.[20,21] It is not unlikely that patients in this group also reduced their breathing rate in response to the music, as has been reported in other studies.[20] Unfortunately, we were unable to monitor the breathing rate for the Walkman group in the present experimental setting. The additional BP reduction produced by the BIM could be attributed to the active breathing exercises. It is not unlikely that part of the observed BP reduction could be attributed to the frequent attention of the medical staff equally given to both groups. The small BP drop that occurred after enrolment and prior to the delivery of the devices may reflect a placebo effect similar for both groups, associated with the patient's expectation to benefit from the intervention.[23]

The observed placebo effect raises a basic methodological issue concerning the appropriate choice of the baseline period, whether it should be the period ending at enrolment or the period prior to the delivery of the device. We believe that an outcome should be measured between two periods during which the variable examined, which determines the study outcome, displays relative stability. This placebo effect is dynamic by nature and it is unclear for what period of time this effect continues. It is possible that after a 2-month period the placebo effect has diminished or completely disappeared. The dynamic changes which are likely to take place before treatment in our experimental setting methodologically preclude using this 'prior to treatment' measurement as the baseline. We therefore calculated the BP change as the difference between the measurement on enrolment and the 'end value' where the latter was calculated as the average BP level during the last 5 weeks of treatment during which BP reached a plateau. Since home BP as well as 24-h ambulatory measurements have been demonstrated to be insensitive to placebo effects,[24] further assessment of our results need to be made using the above methodology.

Regression to the mean was not expected to contribute significantly to the observed BP changes in either group. Such an effect is unlikely when the baseline value is obtained by averaging a number of

measurements.[25] The same can be concluded if a baseline value does not differ significantly from an average based on a number of previous measurements as in the first study, in which the BP data of all 28 enrolled patients was known 1-year prior to enrolment value (average of 6.4 measurements per patient during the year). The BP differences between the enrolment value and the previous year's average were found to be insignificant ($P \geqslant 0.4$ analysed by paired *t*-test) having a Gaussian distribution with an average of –0.3/1.0 mm Hg.

Slow and regular breathing, below 10 breaths per minute, is known to affect reflex control of the cardiovascular system and to modulate BP.[11,12,26–29] More specifically, lung inflation, which increases with decreasing breathing rate, stimulates slowly adapting pulmonary stretch receptors.[11,12] This neural activity serves as an input to the medulla and is integrated with the information about BP level generated by the arterial baroreceptors.[28] As an acute response to BP elevation and/or lung inflation, heart rate is decreased[25–27] and vasodilatation occurs in a number of vascular territories, such as the limbs, skin, muscles, kidney and splanchnic vascular bed.[11,12] Our measurements of the end breathing rate at home and other tests done with the BIM technology[13] demonstrate that breathing at a rate below 10 per minute is easily achievable. The effect of chronic stress on the development of hypertension is rationalised by frequent stress-induced arteriolar vasoconstriction that leads to an adaptive process of thickening and stiffening of arteriolar wall.[30] Three months of mental relaxation with breathing exercises at home significantly blunt the excitatory autonomic changes produced by stress stimuli, similar to β-adrenergic blockade.[31] This evidence, in addition to the acute cardiovascular response to slow breathing mentioned above, suggests that routine sessions of slow and regular breathing may reverse the process that leads to the development of hypertension. A similar rationale has been proposed to explain the benefit of regular walking, which has been shown to produce a reduction in BP.[32] However, the continued beneficial effect of routine breathing exercise and the mechanism involved require further investigation.

The fact that BP levels, measured 6 months after treatment had been terminated, were still significantly lower in the BIM group than on enrolment suggests a residual long-term effect of the BIM treatment on the BP control system. Some behavioural treatments, which applied breathing exercises for treating high BP found residual effects even after 1 year of follow-up.[5,10]

A potential weakness of our study was that it was carried out sequentially, having been completed at clinic site I before continuing in clinic sites II and III. However, bias was largely averted by the blinding of the doctors in the clinical sites as to the treatment device used.

In conclusion, breathing modulation may have therapeutic potential as a low-risk, adjunctive therapy for hypertension. In this study clinically significant BP reductions were observed within 2 months of daily self-treatment with the BIM. The BIM treatment group was shown to have a slower than normal breathing rate at the end the treatment sessions. The slow and regular breathing may play a role in the treatment of high BP. Despite the encouraging results, a larger study including home BP measurements is required in order to confirm these preliminary findings. Additional efforts should also be invested in establishing the underlying mechanisms and optimising this novel non-pharmacological approach.

Acknowledgements

We thank Prof Camil Fuchs from Tel Aviv University and Technostat Ltd for helping with the data analysis, as well as Ehud Cohen and Marla Clayman for their technical assistance. This study was sponsored by InterCure Ltd where Dr Benjamin Gavish is the Chief Scientist.

This study has been previously presented in two congresses.[33,34]

References

1 The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med* 1997; **157**: 2413–2446.
2 Patel C. Yoga and biofeedback in the management of hypertension. *Lancet* 1973; **II**: 1053–1055.
3 Kikuchi T, Ishikawa H. Respiratory control in hypertension. *Cur Biofeedback Res in Japan* 1993; 64–71.
4 Bali LR. Long-term effect of relaxation on blood pressure and anxiety levels of essential hypertensive males: A controlled study. *Psychosom Med* 1979; **41**: 637–646.
5 Patel C. 12-month follow-up of yoga and biofeedback in the management of hypertension. *Lancet* 1975; **I**: 62–64.
6 Patel C, North WRS. Randomised controlled trial of yoga and biofeedback in management of hypertension. *Lancet* 1975; **II**: 93–95.
7 Patel C, Marmot MG, Terry DJ. Controlled trial of biofeedback-aided behavioural methods in reducing mild hypertension. *BMJ* 1981; **282**: 2005–2008.
8 Patel C *et al*. Trial of relaxation in reducing coronary risk: four year follow-up. *BMJ* 1985; **290**: 1103–1106.
9 Irvine MJ, Johnston DW, Jenner DA, Marie GV. Relaxation and stress management in the treatment of essential hypertension. *J Psychosom Res* 1986; **30**: 437–450.
10 Chesney MA, Black GW, Swan GE, Ward MM. Relaxation training for essential hypertension at the worksite: I. The untreated mild hypertensive. *Psychosom Med* 1987; **49**: 250–263.
11 Daly M de B. Interactions between respiration and circulation. In: Cherniack NS, Widdicombe JG (eds). *Handbook of Physiology*. Am Physiol Soc: Bethesda, 1986, pp 529–594.
12 Daly M de B. Aspects of the integration of the respiratory and cardiovascular system. In: Jordan D, Mar-

shall J (eds). *Cardiovascular Regulation*. Portland Press: London, 1995, pp 15–35.
13 Gavish B. Self-regulation of respiration using interactive music in a closed loop. In: Kikuchi T, Sakura H, Saito I, Tsuboi K (eds). *Biobehavioural self-regulation*. Springer-Verlag: Tokyo, 1995, pp 386–390.
14 MacMahon S *et al*. Blood pressure, stroke, and coronary heart disease. *Lancet* 1990; **335**: 765–774.
15 Pyorala K *et al*. Prevention of coronary heart disease in clinical practice. *Eur Heart J* 1994; **15**: 1300–1331.
16 Dengel DR, Galecki AT, Hagberg JM, Pratley RE. The independent and combined effects of weight loss and aerobic exercises on blood pressure and oral glucose tolerance in older men. *Am J Hypertens* 1998; **11**: 1405–1412.
17 Midgley JP, Matthew AG, Greenwood CMT. Effect of reduced dietary sodium on blood pressure: a meta-analysis of randomized controlled trials. *JAMA* 1996; **275**: 1590–1597.
18 Hatch JP. Controlled group designs in biofeedback research: Ask, 'What does the control group control for?'. *Biofeedback and Self-Regulation* 1982; **7**: 377–390.
19 Eisenberg DM *et al*. Cognitive behavioural techniques for hypertension: are they effective? *Ann Intern Med* 1993; **118**: 964–972.
20 White JM. Effect of relaxing music on cardiac autonomic balance and anxiety after acute myocardial infarction. *Am J Crit Care* 1999; **8**: 220–230.
21 Mockel M *et al*. Immediate physiological responses of healthy volunteers to different types of music: cardiovascular, hormonal and mental changes. *Eur J Appl Physiol* 1994; **68**: 451–459.
22 Benson H, Rosner BA, Marzetta BR, Klemchuk HM. Decreased blood-pressure in pharmacologically treated hypertensive patients who regularly elicited the relaxation response. *Lancet* 1974; **I**: 289–291.
23 Agras WS, Horne M, Taylor CB. Expectation and the blood-pressure-lowering effect of relaxation. *Psychosom Med* 1982; **44**: 389–395.
24 Asmar R *et al*. Repeated measurements of non-invasive ambulatory blood pressure: distinction between reproducibility and the proper effect of placebo. *Blood Press Monit* 1996; **1**: 283–288.
25 Davis CE. The effect of regression to the mean in epidemiologic and clinical studies. *Am J Epidemiol* 1976; **104**: 493–498.
26 Pitzalis MV *et al*. Effect of respiratory rate on the relationship between RR interval and systolic blood pressure fluctuations: a frequency-dependent phenomenon. *Cardiovasc Res* 1998; **38**: 332–339.
27 Novak V, Novak P, de Champlain J, Nadeau R. Altered cardiorespiratory transfer in hypertension. *Hypertension* 1994; **23**: 104–113.
28 Cooke WH *et al*. Controlled breathing protocols probe human autonomic cardiovascular rhythms. *Am J Physiol* 1998; **274**: H709–H718.
29 Langhorst P, Schulz G, Lambertz M. Integrative control mechanisms for cardiorespiratory and somatomotor functions in the reticular formation of the lower brain stem. In: Grossman P, Janssen KHL, Vaitl D (eds). *Cardiorespiratory and Cardiosomatic Psychophysiology*. Plenum Press: New York, 1983, pp 9–37.
30 Folkow B. Physiological aspects of primary hypertension. *Phys Rev* 1982; **62**: 347–504.
31 Lucini D *et al*. A controlled study of the effects of mental relaxation on autonomic excitatory responses in healthy subjects. *Psychosom Med* 1994; **59**: 541–552.
32 Tanaka H, Reiling MJ, Seals DR. Regular walking increases peak limb vasodilatory capacity of older hypertensive humans: implications for arterial structure. *J Hypertens* 1998; **16**: 423–428.
33 Schein M *et al*. Non-drug hypertension reduction by device-guided breathing exercises: A double-blind randomized study. *J Hypertens* 1998; **16** (Suppl): S217.
34 Schein M *et al*. Self-treatment of hypertension with device-guided breathing exercises: a double-blind randomized study. *Am J Hypertens* 1999; **12**: 25A.