

The Effect of Different Modalities of Mindfulness-Based Interventions on Blood Pressure

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Abstract

Background: Hypertension is one of the major killers around the world resulting in 7.6 million deaths and 92 million disability-adjusted life years (DALYs) per year. Mindfulness-based interventions (MBIs) have been studied as nonpharmacological modalities of lowering blood pressure. However, the evidence about the different modalities of MBIs is still unclear.

Purpose: The aim of this review is to identify the evidence about the effect of different MBIs on lowering blood pressure among different populations including hypertensive patients and healthy individuals.

Methods: Pubmed, Cochrane Central Register of Controlled Trials (Ovid) and EBSCO databases were systematically used to search by using the keywords "(mindfulness) AND (blood pressure)". All trials published from 1989 to July 2021 that reported the effect of MBIs on blood pressure as primary or secondary outcomes were included. Trials that did not report their results in English were excluded. Titles and abstracts were first screened for eligibility. Eligible studies were then fully reviewed and summarized.

Results: A total of 53 research articles were included in this review with 3947 participants. They include patients with hypertension, cardiovascular diseases, obesity, cancer, stress, diabetes, pregnancy and healthy individuals. Articles were classified and sorted according to the modality of MBI used for better comparison.

Conclusion: MBI modalities that are instructor guided and include breathing and/or physical exercises might result in a significant reduction of BP, especially among patients with HTN and/or anxiety. This effect could be complemented by other pharmacological and non-pharmacological interventions.

Keywords: alternative medicine.symi; blood pressure; hypertension; mindfulness; non-pharmacological.

Introduction

Hypertension is one of the major killers around the world resulting in 7.6 million deaths and 92 million disability-adjusted life years (DALYs) per year (Lawes et al., 2001). Many pharmacological and nonpharmacological management modalities have been developed over the years to control blood pressure (BP). Although often good control cannot be achieved without medications, most practitioners and patients prefer to start with non-pharmacological modalities; including -but not limited to- Dietary Approaches to Stop Hypertension (DASH), exercise ...etc.

Mindfulness can be defined as one's ability to focus their own attention on the current moment. Mindfulness-based interventions (MBIs) have been increasingly gaining attention in the last few decades. Although mindfulness meditation is an ancient practice, several MBIs protocols have been developed in the last 40 years; including Mindfulness-Based Stress Reduction (MBSR) which was developed by Kabat-Zinn (1990), and Mindfulness-Based Cognitive Therapy (MBCT) by Segal, Williams and Teasdale (2002). These modalities are originally developed to manage stress and depression.

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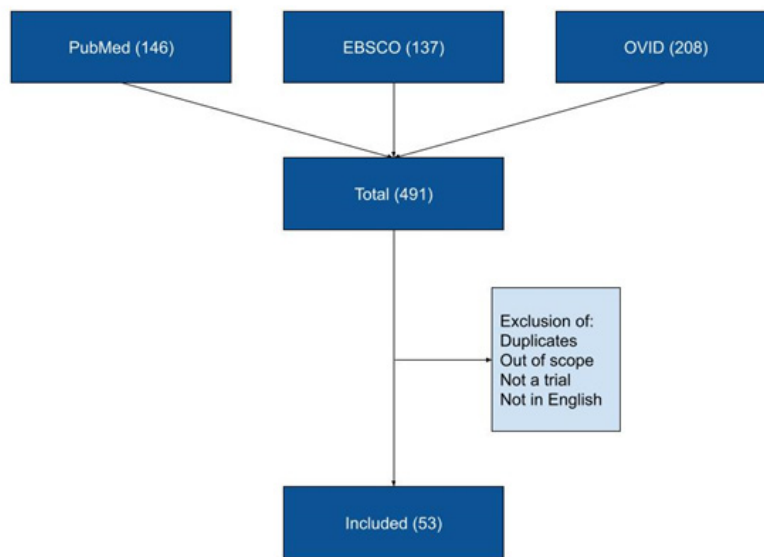


Figure 1. Eligible Studies

However, recently many researchers have been interested in the effect of MBIs on lowering blood pressure among hypertensive patients and healthy individuals. Several review articles showed that MBIs might result in a significant reduction of blood pressure among patients with hypertension and cardiovascular diseases (Marino et al., 2021; Conversano et al., 2021; Verma et al., 2021; Zou et al., 2021). On the other hand, other review articles reported no significant effect among similar populations (Ahmadpanah et al., 2016).

The aim of this review is to identify the evidence about the effect of different MBIs on lowering blood pressure among different populations including hypertensive patients and healthy individuals.

Methods

Design

This study was conducted as a narrative review.

Search methods

A systematic search was conducted using PubMed, Cochrane Central Register of Controlled Trials (Ovid) and EBSCO databases. The keywords were "(mindfulness) AND (blood pressure)". Titles and abstracts were first screened for eligibility. Eligible studies were then fully reviewed and summarized (Figure 1).

Inclusion and exclusion criteria

All trials published from 1989 to July 2021 that reported the effect of MBIs on blood pressure as primary or secondary outcomes were included. Trials that did not report their results in English were excluded.

Results

A total of 53 research articles were included in this review with 3947 participants. These participants were mostly adults with a variation in their ages. They include patients with hypertension, cardiovascular diseases, obesity, cancer, stress, diabetes, pregnancy and healthy individuals. Articles were classified and sorted according to the modality of MBI used for better comparison (Table 1).

MBSR

Two studies including 157 participants with unmedicated prehypertension and stage 1 hypertension were conducted for 8 weeks. Among prehypertensive patients, MBSR resulted in a significant reduction of SBP and DBP when compared to progressive muscle relaxation training (Hughes et al., 2013). On the other hand, MBSR did not result in a significant reduction of SBP and DBP among unmedicated stage 1 hypertension when compared with a wait-list control group. However, "in the secondary analysis, there was a small significant within-group reduction in BP for the entire cohort pre- to postintervention. This effect was largely confined to female subjects" (Blom et al., 2014). Additionally, a study of 42 participants with high-normal BP and stage 1 hypertension resulted in a significant reduction of SBP and DBP when compared to the control group (Ponte et al., 2018). Furthermore, MBSR significantly reduced both SBP and DBP even after 8 weeks of intervention cessation in adults with HTN (Nejati et al., 2015).

Four trials were conducted including 249 patients with CHD, cardiac events, and cardiac diseases. Three of these trials stated that MBSR resulted in a significant reduction in SBP when compared to control (Parswani et al., 2013; Momeni et al., 2016; Gu & Zhu, 2018). However, the fourth trial showed no significant effect of MBSR on SBP when compared with control at 3 and 9 months (Nijjar et al., 2019).

Two studies among 280 adults with obesity

Table 1. Articles Summary

Reference	Year	Population	Sample Size	Modality	Inter-vention duration	Main Relevant Results
Hughes et al.	2013	Adults with unmedicated prehypertensive BP	56	MBSR	8 weeks	MBSR resulted in a significant reduction of SBP and DBP when compared to progressive muscle relaxation training.
Blom et al.	2014	Unmedicated stage 1 hypertension patients	101	MBSR	8 weeks	MBSR did not result in a significant reduction of SBP or DBP when compared with a wait-list control group. However "in the secondary analysis, a small but significant within-group decrease in BP was observed for the entire cohort from pre- to postintervention. This effect was largely confined to female subjects."
Ponte Márquez et al.	2018	Adults with high-normal BP or grade 1 hypertension	42	MBSR	8 weeks	MBSR resulted in a significant reduction of SBP and DBP compared to control.
Nejati et al.	2015	Adults with HTN	30	MBSR	8 weeks	MBSR resulted in significant reductions in both SBP and DBP. This reduction was maintained after 8 weeks of intervention cessation.
Parswani et al.	2013	male patients with CHD	30	MBSR	8 weeks	MBSR resulted in a significant reduction of SBP compared to control.
Momeni et al.	2016	Cardiac patients	60	MBSR	8 weeks	MBSR resulted in a significant reduction of SBP compared to control.
Gu & Zhu	2018	Patients with stable coronary heart disease	112	MBSR	12 weeks	MBSR resulted in significantly larger reductions in SBP when compared to control.
Nijjar et al.	2019	Adults with with a cardiac event or procedure	47	MBSR	8 weeks	This pilot study showed no significant difference in BP between MBSR and control at 3 and 9 months
Daubenmier et al.	2016	Adults with obesity	194	MBSR	5.5 months	There was no significant difference between MBSR + diet-exercise guidelines, and diet-exercise guidelines only in their effect on BP.
Raja- Khan et al.	2017	women with overweight or obesity	86	MBSR	8 weeks	MBSR did not result in a statistically significant reduction of SBP or DBP after 8 weeks
Kopf et al.	2014	Type 2 Diabetes Patients with Early Kidney Disease	110	MBSR	8 weeks	MBSR resulted in a significant reduction of SBP and MAP for up to one year. However, this effect was not significant after 2 or 3 years.
Palta et al.	2012	Low-income African-American older adults	20	MBSR	8 weeks	MBSR resulted in a significant reduction of SBP and DBP when compared to control.
Manigault et al.	2018	Adults with moderate to high perceived stress	72	MBSR	6 weeks	The MBSR group showed a significantly greater reductions in MAP compared to CBT and waitlist control groups.

Cont. Table 1. Articles Summary

Reference	Year	Population	Sample Size	Modality	Inter-vention duration	Main Relevant Results
Nyklíček et al.	2013	adults with stress-related complaints	85	MBSR	8 weeks	MBSR group reported significantly lower SBP and DBP than the control at rest, during exposure to stress and after recovery.
Manigault et al.	2021	healthy adults reporting moderate/high stress	86	MBSR	6 weeks	There was no significant difference between MBSR, CBT and control groups in blood pressure habituation after stress.
Matchim et al.	2010	Breast cancer survivors	36	MBSR	8 weeks	There was a significant difference between MBSR and control in reducing both SBP and DBP.
Oswald et al.	2021	Young adult cancer survivors	126	MBSR	8 weeks	MBSR resulted in a significant reduction of SBP and DBP over time.
Campbell et al.	2012	Women with cancer	76	MBSR	8 weeks	There was no significant difference between MBSR and waitlist control groups.
Amutio et al.	2015	physicians	42	MBSR	8 weeks (weekly sessions) + 10 months (monthly sessions)	MBSR resulted in significant reductions in both SBP and DBP. This reduction was maintained after 12 months of intervention and was positively correlated to the total number of hours of home practice.
Kalinowski et al.	2021	women with pre-hypertension	37	telephone-delivered mindfulness-based cognitive therapy (MBCT-T)	8 weeks	There was no significant difference between reductions of BP among MBCT-T and control groups.
Alamout et al.	2020	women with overweight	45	Energy-restricted diet therapy with MBCT	8 weeks	MBCT with diet therapy resulted in significantly greater reductions in SBP compared to diet therapy alone. However, this effect was not significant on DBP.
Shay et al.	2018	Pregnant women	61	MBCT	8 weeks	There was no significant difference between MBCT and treatment as usual groups.
Bostock et al.	2018	employees at two U.K. companies	238	Headspace (smartphone meditation application)	45 days	There was no significant effect of mobile-based mindfulness training on BP compared to control
Aitè et al.	2019	Adult patients diagnosed with Somatoform Autonomic Dysfunction of cardiological	29	Online Mindfulness-based meditation exercise. (based on MBSR and MBCT)	3 weeks	There was no significant difference between Online Mindfulness-based meditation exercises and control in their effect on BP.
system	29	system	29	Online Mindfulness-based meditation exercise. (based on MBSR and MBCT)	3 weeks	There was no significant difference between Online Mindfulness-based meditation exercises and control in their effect on BP.
Younge, Wery, et al.	2015	Adults with heart disease	324	Online mindfulness meditation program	12 weeks	There was no significant difference between the online mindfulness meditation program and usual care in reducing BP after 3 months

Cont. Table 1. Articles Summary

Reference	Year	Population	Sample Size	Modality	Inter-vention duration	Main Relevant Results
Lindsay et al.	2018	Adults with stress symptoms	144	monitoring and acceptance (smartphone application)	3 weeks	Monitoring and acceptance resulted in a significant reduction of SBP during stress and in recovery compared to monitoring only and control groups. However, there was no significant effect on DBP.
Rajendran et al.	2020	Patients with uncontrolled hypertension	76	MINDING-GOALS program	16 weeks	Reductions in SBP and DBP in the MINDING-GOALS group were not significantly different from those in the GOALS group.
Creswell et al.	2014	college students	66	Brief mindfulness meditation training (recorded)	3 days (25-min per day)	There was no significant effect of the brief mindfulness meditation training on SBP or DBP during response and recovery from stress.
Miller et al.	2021	Adolescents at-risk for adult obesity	29	Mindfulness-induction	once (10 min)	There was no significant effect of mindfulness induction on SBP or DBP.
Grant et al.	2011	college students with a family history of HTN	97	Mindfulness-Analog (recorded)	one session (20 min)	Participants in the mindfulness group had slower and reduced rates of BP recovery after stress than participants in the control group
Coelho et al.	2018	women undergoing breast biopsies	82	Mindfulness-based body scan (recorded)	1 week	MBBS group reported significantly lower mean SBP and DBP compared to control; measured at one instance only
Park et al.	2014	African-American male veterans with HTN and CKD Stage III	15	Prerecorded guided mindfulness meditation (MM)	Once (14 min)	Mindfulness meditation resulted in a significant acute reduction of SBP and DBP compared to control. These reductions were sustained for at least several minutes post-MM.
Gainey et al.	2016	Adults with type 2 diabetes	27	Buddhist walking meditation	12 weeks	There was a significant difference in reducing SBP and DBP among diabetic patients using Buddhist walking meditation exercises when compared to traditional walking exercises.
Roche et al.	2017	older adults with HTN	55	Himalayan Yoga Tradition Meditation	8 weeks	Himalayan Yoga Tradition Meditation resulted in a significant reduction of SBP when compared to other forms of Yoga and control.
Hilcove et al.	2020	Healthcare practitioners	80	Mindfulness-Based Yoga	6 weeks	There was no significant change in SBP or DBP over time in Mindfulness-Based Yoga and control groups.
Ng et al.	2016	Cancer patients under palliative care	60	mindful breathing	one session (5 min)	Mindful breathing resulted in a significant reduction of both SBP and DBP compared to control.
Mitsunagnern et al.	2021	Patient with hypertensive urgency	110	Pursed-lip breathing with number counting	3 hours (15 minutes per hour)	Pursed-lip breathing with number counting resulted in a significant reduction of both SBP and DBP compared to control.

Cont. Table 1. Articles Summary

Reference	Year	Population	Sample Size	Modality	Intervention duration	Main Relevant Results
Chesney et al.	2016	pre-hypertensive, post-menopausal women	95	Mindful breathing (MB)	8 weeks	MB resulted in a large significant reduction of SBP when compared to control. However, no significant difference was noticed in DBP.
Ahmadpanah et al.	2014	women with HTN	45	(Metacognitive detached mindfulness therapy) and (Stress management training)	8 weeks	Both metacognitive detached mindfulness therapy and stress management training resulted in significant reductions of both SBP and DBP when compared to control. However there was no significant difference between the two intervention groups.
Wright et al.	2020	Hypertensive African Americans	38	Mindfulness in Motion and Dietary Approaches to Stop Hypertension DASH (MIM DASH)	8 weeks	There was a significant reduction in SBP in the MIM DASH group when compared to the attention only group
Mohammadi et al.	2021	Adults with type 2 diabetes	30	Mindful Breath Awareness and Muscle Relaxation (MBMR), transcranial electrical stimulation (tCES)	2 weeks	"MBMR treatment was more effective than the tCES with more than 95% confidence to decrease the systolic blood pressure in the post-intervention. However, the MBMR intervention and the MBMR+tCES treatment had the same effects on decreasing the systolic blood pressure in the post-intervention. Furthermore, the tCES intervention and the MBMR+tCES treatment also had the same effects on decreasing the systolic blood pressure in the post-intervention."
Chen et al.	2012	first-year nursing students	60	Mindfulness meditation training	7 consecutive days	Mindfulness meditation training resulted in a significant reduction of SBP compared to control. However, there was no significant effect on DBP.
Alexander et al.	1989	elderly	73	Transcendental Meditation (TM) program, mindfulness training (MF), relaxation program.	3 months	TM and MF groups showed lower posttest mean SBP after 3 months when compared with relaxation and control groups.
Crosswell et al.	2017	breast cancer survivors	71	Mindful Awareness Practices (MAPs)	6 weeks	MAPs resulted in a significantly lower DBP at the recovery stage from stress. However, no significant difference was reported between MAPs and control groups in SBP.
Muthukrishnan et al.	2016	Pregnant women of 12 weeks gestation	74	Mindfulness meditation program	5 weeks	The mindfulness meditation program resulted in significantly lower SBP and DBP responses to cold pressure when compared to control.

Cont. Table 1. Articles Summary

Reference	Year	Population	Sample Size	Modality	Inter-vention duration	Main Relevant Results
Ditto et al.	2006	healthy young adults	32	Body scan meditation	4 weeks	There was no significant difference between body scan meditation and progressive muscular relaxation in their effect on BP.
Wolever et al.	2012	Employees of an insurance carrier	239	Mindfulness at Work program	12 weeks	There was no significant difference between the Mindfulness at Work program, Yoga and control in their effect on BP.
Kingston et al.	2007	University students	42	Mindfulness meditation program	3 weeks	There was no significant difference between the Mindfulness meditation program and Guided Visual Imagery in their effect on BP.
Eisenberg et al.	2019	Employees of culinary school	40	Teaching Kitchen (TK) self-care intervention (offers the combination of culinary, nutrition, exercise, and mindfulness instruction with health coaching)	14 or 16 weeks	TK resulted in a significant reduction of SBP and DBP comparing baseline and post intervention levels.
Johnson et al.	2019	college students	75	5 minutes of mindfulness meditation (MM)	once	MM group showed significantly lower BP reactivity to speech and anger recall than the control group.
Ee et al.	2020	Patients with type 2 diabetes	18	Shared medical appointments with mindfulness training	12 weeks	Adding mindfulness training to shared medical appointments did not result in significantly different reductions of SBP or DBP compared to usual care which included recommending using a free mindfulness app.
Shilling et al.	2017	Women with breast cancer	29	Self-guided mindfulness	8 weeks	Self-guided mindfulness resulted in a significant reduction of SBP compared to baseline measures of the same group.

BP: Blood pressure.

MBSR: Mindfulness-based stress reduction.

SBP: Systolic blood pressure.

DBP: Diastolic blood pressure.

HTN: Hypertension.

CHD: Coronary heart disease.

MAP: Mean arterial pressure.

MBCT: Mindfulness-based cognitive therapy.

CKD: Chronic kidney disease.

showed that MBSR has not significantly reduced SBP when compared to control (Daubenmier et al., 2016; Raja-Khan et al., 2017).

A trial was conducted on 110 participants with type 2 diabetes and early kidney disease showed that MBSR resulted in a significant reduction in SBP and mean arterial pressure (MAP), and this reduction continued for up to one year. However, there were no significant results after that (Kopf et al., 2014).

Four studies were conducted among adults with stress-related complaints. The first two studies reported that MBSR significantly reduced BP compared with control (Palta et al., 2012; Manigault et al., 2018).

The third study showed that the MBSR group had significantly lower SBP and DBP compared to the control one when they were exposed to stress and at rest (Nyklíček et al., 2013). On the other hand, the fourth study showed that there was no significant difference between

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MBSR, CBT and control groups in blood pressure habituation after stress (Manigault et al., 2021).

Two out of three studies including 238 cancer patients and survivors showed significant reductions in BP after MBSR (Matchim et al., 2010; Oswald et al., 2021) while the third one showed no significant difference between MBSR and waitlist control groups (Campbell et al., 2012).

Authors of one trial including 42 physicians reported that MBSR resulted in a significant reduction of both SBP and DBP after 12 months of the intervention. These results were positively correlated with the home practice hours (Amutio et al., 2015).

MBCT

MBCT was investigated in three studies involving 143 participants. Two of these studies showed no significant difference between MBCT and control groups of women with prehypertension or pregnancy (Kalinowski et al., 2021; Shay et al., 2018). On the contrary, the third study showed that MBCT with diet therapy resulted in significantly greater reductions of SBP compared to diet therapy alone among overweight women. However, this effect was not significant on DBP (Alamout et al., 2020).

Online/smartphone application mindfulness training

Five studies including 811 participants were conducted using websites or smartphone applications to deliver mindfulness training. Three studies carried out for 3, 6 and 12 weeks showed no significant effect of mindfulness training on BP over control. The participants in these studies were healthy or had cardiovascular diseases (Bostock et al., 2019; Younge et al., 2015; Gotink et al., 2017). Furthermore, a study of the effect of adding a mindfulness component to an online self-help program designed for hypertensive patients showed no significant difference between the two groups of intervention; with and without the mindfulness component (Rajendran et al., 2020). However, one study conducted with adults who experience stress symptoms reported a significant reduction in SBP only; following 3 weeks of mindfulness training in the form of monitoring one's own experience and accepting it (Lindsay et al., 2018).

Recorded mindfulness meditation

Authors of five trials involving 289 participants used prerecorded audio or video clips to guide the participants through sessions of mindfulness meditation. These sessions varied in duration and frequency. They lasted from 10–25 minutes and were conducted once, for three consecutive days or for a week. Two studies involving healthy college students and adolescents at risk of obesity showed no significant effect of listening to a prerecorded mindfulness meditation on BP (Creswell et al., 2014; Miller et al., 2021).

Furthermore, one trial showed that college students with family history of HTN who were exposed to 20 minutes of Mindfulness-Analog audiotape had

slower and reduced rates of BP recovery after stress when compared with participants in the control group (Grant et al., 2013).

However, one study reported that women undergoing breast biopsies had lower baseline SBP and DBP after listening to mindfulness-based body scan audio tapes for a week when compared to controls (Coelho et al., 2018). Moreover, one trial showed that mindfulness meditation for 14 minutes resulted in a significant acute reduction of SBP and DBP when compared to control among African-American male veterans with HTN and CKD Stage III. These reductions were sustained for at least several minutes post-MM (Park et al., 2014).

Active mindfulness meditation

Three studies were conducted with 162 participants using different forms of active mindfulness exercises. Two studies reported a significant reduction of BP among adults with type 2 diabetes and HTN after using Buddhist walking meditation for 12 weeks and Himalayan Yoga Tradition Meditation for 8 weeks respectively when compared to control (Gainey et al., 2016; Tolbaños Roche et al., 2017).

However, practicing Mindfulness-Based Yoga for 6 weeks did not result in a significant change in BP among healthcare practitioners (Hilcove et al., 2021)

Brief mindful breathing

Most mindfulness meditation exercises include focusing on breathing as an anchor for one's attention. However, in two studies, the authors implemented brief mindful breathing (MB) exercises only with 60 cancer patients under palliative care and 110 patients suffering from hypertensive urgency. Both studies reported a significant reduction of BP immediately after interventions when compared to control (Ng et al., 2016; Mitsungrern et al., 2021). Furthermore, one study of 95 pre-hypertensive, post-menopausal women showed that MB resulted in significantly larger reductions of SBP when compared to the control group. However, no significant difference was noticed in DBP (Chesney et al., 2016).

Other modalities

The authors of the remaining 14 studies conducted different modalities of MBIs involving 866 participants. Two studies reported that MBIs resulted in a significant reduction of BP among women and African-American men with HTN (Ahmadpanah et al., 2016; Wright et al., 2021).

In the first study, there was no significant difference between metacognitive detached mindfulness therapy and stress management training in their effect on BP (Ahmadpanah et al., 2016). Furthermore, in the second study Mindfulness in Motion was complemented by Dietary Approaches to Stop Hypertension (Wright et al., 2021).

When compared to baseline, one study showed that Teaching Kitchen (TK) self-care intervention (offers the combination of culinary, nutrition,

exercise, and mindfulness instruction with health coaching) resulted in a significant reduction of SBP and DBP (Eisenberg et al., 2019).

Four studies showed that MBIs resulted in a significant reduction of SBP only but had no significant effect on DBP among adults with type 2 diabetes, nursing students, elderly people and women with breast cancer (Mohammadi et al., 2021; Chen et al., 2013; Alexander et al., 1989; Shilling et al., 2017).

On the contrary, one study reported a significant reduction of DBP only among breast cancer survivors (Crosswell et al., 2017).

Two studies showed that mindfulness meditation resulted in significantly lower SBP and DBP reactivity to induced stress when compared to control among pregnant women and college students (Muthukrishnan et al., 2016; Johnson et al., 2019).

Finally, three studies reported that there was no significant difference between MBIs and controls in their effect on BP among healthy adults and diabetic patients (Ditto et al., 2006; Wolever et al., 2012; Kingston et al., 2007; Ee et al., 2020).

Discussion

The majority of studies, 13 out of 19, that examined the effect of MBSR on blood pressure showed significantly greater reductions when compared to control. These results are consistent with the result of other reviews (Verma et al., 2021; Intarakamhang et al., 2020; Conversano et al., 2021; Priya & Kalra, 2018; Solano López, 2018; Abbott et al., 2014; Younge, Gotink, et al., 2015). However, this effect was not as salient with the studies that addressed MBCT, online/smartphone application mindfulness training or recorded mindfulness meditation, since the ratios of studies with significant reduction of BP to studies with no significant reduction of BP were 1:2, 1:4 and 2:3, respectively.

On the other hand, mindfulness modalities that focus on breathing (3 out of 4 studies) or add physically active (2 out of 3) components were shown to result in more reductions in BP when compared to control.

Overall, the use of an MBI of any modality for individuals with HTN or anxiety showed significantly greater reductions in BP in a ratio of 3:1.

Since this is a narrative review, it has some strengths and limitations. One strength would be the relatively wide scope which resulted in more studies being included in the review. However, the results showed be considered with caution because of the heterogeneity of the studies and the lack of quality assessment.

Conclusion

This review suggests that the effect of MBIs on BP varies greatly based on the modality used. Overall, MBI modalities that are instructor guided and include breathing and/or physical exercises might result

in a significant reduction of BP especially among patients with HTN and/or anxiety. This effect could be complemented by other pharmacological and non-pharmacological interventions. More research is needed to study the long-term effects of MBIs.

Declaration of Interest

The authors have no conflicts of interest to declare.

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