ORIGINAL ARTICLE

Impact of a Meditation Program on Pulse-Wave Velocity, C-Reactive Protein and Quality of Life

Impacto de un programa de meditación sobre la velocidad de onda de pulso, la proteína C-reactiva y la calidad de vida

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ABSTRACT

Background: Although various studies refer to the effect of meditation on blood pressure (BP), its impact on other cardiovascular clinical variables is unknown.
Objective: The aim of this study was to evaluate the effects of a meditation program on pulse wave velocity (PWV), quality of life and ultrasensitive C-reactive protein (us-CRP) in patients with ischemic heart disease or chronic heart failure.
Methods: This was a randomized study with two groups of patients: a meditation group (M) and an active control group (AC) with cardiovascular health education, evaluating the difference between initial and final values at 12 weeks of BP, PWV, quality of life (assessed by the SF-36 questionnaire) and us-CRP.
Results: Thirty-five patients were included in the M group and 35 in the AC group; mean age was 61 years and 80% were men. Both groups had similar baseline characteristics, except for higher number of smokers and triglyceride levels in the M group. At 12 weeks, no significant differences were found for ΔPWV: +0.51 (±1.40) in AC and +0.19 (±1.53) in M (p=0.37). Conversely, ΔSF-36 was +0.79 (±7.58) in AC vs. +5.40 (±9.69) (p=0.03) in M, and Δus-PCR was +1.17 (±2.9) in AC vs. -0.69 (±0.89) in M (p=0.02).
Conclusions: A meditation program did not significantly modify PWV at 12 weeks. However, patients allocated to this intervention improved their quality of life and us-PCR was significantly reduced. Larger studies are required to confirm these findings and explore the mechanisms involved in this improvement.

Key words: Meditation - Pulse Wave Analysis - Quality of Life - C-Reactive Protein

RESUMEN

Introducción: Si bien existen publicaciones referentes al efecto de la meditación en la presión arterial (PA), su impacto en otras variables clínicas cardiovasculares, se desconoce.
Objetivos: Evaluar el impacto de un programa de meditación (M) en la velocidad de onda de pulso (VOP), la calidad de vida y la proteína C reactiva ultrasensible (PCRu) en pacientes con cardiopatía isquémica o insuficiencia cardíaca estable.
Métodos: Se realizó un estudio aleatorizado, randomizando en dos grupos de pacientes: M, basada en meditación y control activo (CA) de educación cardiovascular. Se evaluaron diferencias entre valores iniciales y finales a 12 semanas de PA, VOP, calidad de vida (valorado por SF 36) y PCRu.
Resultados: Se incluyeron 35 pacientes en M y 35 en CA, edad media: 61 años, 80% hombres. Las características basales de ambos grupos fueron similares a excepción del mayor número de tabaquistas y triglicéridos más elevados en el grupo de M. Al cabo de 12 semanas, el Delta VOP no tuvo diferencias significativas: + 0,51 (±1,40) en CA y de + 0,19 (± 1,53) en M (p=0,37). El Delta SF 36 fue de + 0,79 (±7,58) vs + 5,40 (±9,69) (p=0,03) en CA y M, respectivamente y el Delta de PCRu fue de + 1,17 (+-2,9) en CA vs -0,69 (+-0,89)en M (p=0,02).
Conclusiones: Un programa de M no modificó significativamente la VOP a 12 semanas. Sin embargo, los pacientes asignados a esta intervención mejoraron su calidad de vida y redujeron su PCRu en forma significativa. Se requieren estudios de mayor tamaño que confirmen estos hallazgos y exploren los mecanismos involucrados en esta mejoría.

Palabras clave: Meditación - Análisis de Onda de pulso - Calidad de vida - Proteína C Reactiva

Abbreviations

AC	Active control	**PWV**	Pulse wave velocity
BMI	Body mass index	**PPA**	Pituitary Pineal Activation
BP	Blood pressure	**TM**	Transcendental meditation
CBP	Central blood pressure	**us-CRP**	Ultrasensitive C-reactive protein
M	Meditation		

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INTRODUCTION

Cardiovascular disease is a major cause of death, mainly due to coronary heart disease and stroke, (1) that equally affects both men and women. It also presents high risk of new cardiovascular events. (2) In this scenario, numerous lifestyle and pharmacological therapeutic options are used to reduce the risk of new events in patients with established cardiovascular disease. Among the non-pharmacological strategies, different studies report the benefits of meditation (M) programs in controlled designs, with significant improvement in blood pressure (BP) levels (3-8) and in the development of atherosclerosis assessed through carotid intima-media thickness. (9) Although most of these studies employed transcendental meditation (TM), (7, 8) there are few published studies on the effects of other types of M, as the one called APP. The aims of this study were: 1) to verify whether an APP-based M program was able to reduce pulse wave velocity (PWV) in patients with established cardiovascular disease, and 2) to analyze the program impact on an inflammatory marker [ultrasensitive C-reactive protein (us-CRP)], other arterial stiffness parameters and quality of life. (10, 11)

METHODS

A prospective, open-label, randomized, controlled study of M versus active control (AC) with cardiovascular education was performed between January and October 2013. It enrolled men and women >21 years, referred from different centers in CABA and Buenos Aires outskirts, with history (more than 3 months) of acute myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft surgery, stable chronic angina or dilated cardiomyopathy/chronic heart failure. In these patients, clinical history, PWV, BP, systolic central blood pressure (CBP), lipid panel, us-CRP and quality of life testing (SF-36) were recorded. Patients were randomized in a simple fashion to M or AC. At week 12, the patients completed again all the measurements. Adherence to the allocated group was evaluated by telephone contact at 4, 8 and 12 weeks.

The primary endpoint was the difference between initial and final PWV (ΔPWV) at week-12 between the two study groups, measured in meters/second (m/s). The secondary endpoints were the difference between initial and final values (Δ) of the following variables: quality of life (SF-36 score), us-CRP in mg/L, CBP in mmHg and BP in mmHg.

M Group

Patients assigned to this group were taken to a facility in Capilla del Señor, Buenos Aires, where they were trained during two days by Alkymia Global instructors specialized in APP meditation (Figure 1). APP meditation is an intervention technique different from TM, based upon activations and connections of the subject with images associated to his/her health, in this case, focused on cardiovascular health. Patients had to practice M twice a day during 20 minutes. After finishing their training period, patients received a CD with a guide of exercises to be performed during the subsequent 12 weeks. Six follow-up group sessions were carried out bimonthly in charge of the Alkymia team to reinforce and go over the techniques. The intervention did not imply any type of patient renunciation to beliefs, creed or religion they held.

AC Group

Patients had to attend health education and cardiovascular prevention workshops lasting 2 hours each, where they received information on cardiovascular risk factors and cardiovascular prevention measures. Six bimonthly educational lectures were given by doctors, emphasizing care concerning healthy habits.

Evaluation of arterial stiffness

All parameters were assessed using TensioMedTM Arteriograph, a validated device of non-invasive medicine. (12-14)

Measurementsare obtained from oscillometric data by occlusion of the brachial artery with a balloon inflated to suprasystolic pressure. Pulse wave velocity indicates the ratio between the distance traveled by the pulse wave (along the arterial wall) between two points of the arterial tree and transit time; its value is directly associated with arterial stiffness, so the higher the PWV, the greater the stiffness. Measurements were performed with the following requirements: (15) patient at rest for at least 5 minutes, in recumbent position, similar time of day to perform the different measurements and interruption of smoking and caffeine-rich beverages at least 3 hours prior to taking measurements. Each arteriograph measurement provided PWV, BP and CBP values. To assess final BP, two BP measurements were performed with mercury sphygmomanometer (in each arm), according to the European guidelines on BP management, (16) which were averaged with the BP values reported by the arteriograph. Measurements were taken in a single center by one operator.

Quality of life test

The SF-36 health survey questionnaire (Argentine adaptation validated from the Spanish version of the test) was used. (17) This is a self-administered questionnaire that covers the perception of an individual on different aspects of his/her health. The final test result provides two scores corresponding to physical and mental health which are added to obtain an overall result. (18, 19) The better the perceived health status, the higher the final score. (20) Each of the two components has a value ranging from 30 (worse) to 70 (better). The mean score for the general population is 50.

Laboratory

Lab testing was centralized and blood samples were withdrawn in the morning after 12-hour fasting. Hematocrit, hemoglobin, platelet count, GOT, GPT, creatinine, urea, sodium, potassium, total cholesterol, HDL-cholesterol, triglyc-

Fig. 1. Meditation training with Alkymia Global instructors

erides, blood glucose, and CPK were measured. LDL-cholesterol was estimated with the Freedwald formula, except for patients with triglycerides >3000 mg/dL, in which case LDL-cholesterol was directly assayed. In two-third of patients, us-CRP was measured by immunoturbidimetry assay.

Statistical analysis

Sample size was established to obtain a difference in PWV variation of 1.5 m/s with±2.2 m/s standard deviation. With these premises 70 patients (35 per group) were required, with $p<0.05$ ($\alpha=5\%$) and 80% power. Ten % additional patients were included to account for possible loses. Simple randomization, 1:1 to AAP or AC, was used. The "intention to treat" analysis was employed. Normal distribution of variables was explored analyzing the mean, standard deviation, skewness, kurtosis and histogram, and using the Shapiro-Wilk test. Continuous data were compared with Student´s t test for normal distribution or the Mann-Whitney-Wilcoxon test for non-normal distribution.

The chi-square test was used to analyze categorical data. Continuous data were expressed as mean±SD and categorical variables as percentages. Blinded statistical analysis was performed by professionals from the Argentine Society of Cardiology, independent from Alkymia Global.

Ethical considerations

The study was approved by the Ethics Committee of the Argentine Society of Cardiology and was performed following the recommendations in medical research suggested by the Helsinki Declaration (21), good clinical practice guidelines and valid ethical regulations.

RESULTS

From a total of 77 patients included in the program, 70 (91%) completed the study. Seven patients abandoned the study before starting any intervention, 4 from the M group and 3 from the AC group. Baseline characteristics (Table 1) were similar for both groups, except for a higher number of smokers and elevated triglyceride levels in the M group (4 patients in M vs. none in AC). The difference in parameter values between both groups is detailed in Table 2.

The primary endpoint, ΔPWV, was not significantly different between the two groups. Baseline PWV values varied from 9.32 m/s (±1.24) to 9.82 m/s (±1.56) at 12 weeks in the AC group ($p=0.06$) and from 9.91 m/s (±1.85) to 10.01 m/s (±1.72) in the APP group ($p=0.45$), with ΔPWV of 0.51 m/s (±1.40) and 0.19 m/s (±1.53) in each group, respectively ($p=0.37$). SF-36 results are detailed in Figure 2. ΔSF-36 was significantly lower in the AC group compared to the M group: +0.79 (±7.58) vs. +5.40 (±9.69), ($p=0.03$). Ultrasensitive-CRP results are illustrated in Figure 3. Baseline and 12-week CBP values in the AC group were 127.43 mmHg (±17.50) and 132.59 mmHg (±15.99), respectively ($p=0.15$), and 136.70 mmHg (±28.32) and 133.63 mmHg (±37.10) ($p=0.57$) in the M group, with ΔCBP of +5.15 mmHg (±20) and -3.07 mmHg (±32) in each group, respectively ($p=0.09$). No significant differences were found between both groups for BP and the remaining parameters over the 12-week period. Median patient adherence was 75% in the M group and 78% in the AC group.

DISCUSSION

Numerous interventions are designed to reduce cardiovascular risk in patients with prior cardiovascular disease. (2) This scenario includes strategies oriented to improve surrogate indicators or variables which have shown to be associated with the risk of clinical events, as PWV, quality of life and us-CRP, among others. (10, 11) Several publications refer to the impact of M programs on cardiovascular manifestations, especially on the practice of TM in the area of hypertension. (3-6) Interesting results from recent randomized studies and meta-analyses compare the practice of M with the use of antihypertensive drugs, and even the American Heart Association released a consensus document, with IIB recommendation and level of evidence B, for different alternative practices and their impact on BP. (7, 8) Our study used an intervention strategy different from TM, based on activations and connections of the subject with images referred to his/her cardiovascular health, and analyzed whether this intervention could reduce parameters associated with arterial stiffness and produce some impact on quality of life and us-CRP. We chose PWV as primary endpoint, as it is an indicator with growing evidence of its association with risk (11) and because up to the present, there are no publications that have investigated the impact of M on this parameter. The literature indicates that PWV and CBP increase with acute and chronic stress, (22) In this framework, a M strategy, able to modulate stress, could reduce these parameters. Since our result was negative, we postulate as possible explanation lack of M efficacy on PWV and insufficient power of our study to demonstrate an impact on this variable. A similar study explored the effect of a TM program in 103 patients with metabolic syndrome. (23) Even though the authors reported several improved clinical and laboratory indicators, TM did not have a favorable impact on endothelial function, a parameter associated to PWV.

Regarding the secondary endpoints of our study, the M group improved their quality of life assessed through the SF-36 questionnaire. (17-20) The overall test score improved in the M and not in the AC group, and the mental component was the main reason for the improvement.

Additionally, patients in the M group significantly reduced us-CRP, a parameter repeatedly associated with the risk of new cardiovascular events. (24, 25) Since during the time of the study there was no change in the drug regimen, body weight or lipid panel in either group, us-CRP reduction in the M group cannot be explained by these factors. A study with a smaller sample size and "before-after" design obtained similar results on the association between improved quality of life assessed with the SF-36 and us-CRP reduction in 24 subjects after 8 weeks of meditation. (26)

Continuous variables	AC (n=35)	M (n=35)	p
Age, years	62.42 (8.57)	60.17 (9.70)	0.31
BMI, kg/mm2	27.51 (3.94)	27.32 (4.08)	0.84
Systolic BP, mmHg	126.61 (15.54)	134.89 (23.77)	0.09
Diastolic BP, mmHg	76.70 (10.38)	78.17 (14.93)	0.64
PWV, m/s	9.32 (1.24)	9.91 (1.85)	0.12
CBP, mmHg	127.43 (17.50)	136.70 (28.32)	0.11
Hematocrit, %	42.65 (4.09)	40.93 (4.59)	0.23
Creatinine, mg/dL	1.25 (1.40)	1.04 (0.24)	0.55
Total cholesterol, mg/dL	150.90 (33.91)	155.47 (24.94)	0.63
LDL-C, mg/dL	93.55 (23.97)	86.27 (22.83)	0.34
Triglycerides, median (interquartile range 25-75), mg/dL	80.5 (70.5-96.5)	120 (80-187)	0.02
HDL-C, mg/dL	46.38 (6.48)	43.11 (11.71)	0.77
us-CRP, mg/L	1.28 (1.42)	1.71 (1.34)	0.36
SF-36, score	106.42 (8.88)	102.51 (10.49) s	0.09
Categorical variables,	**%**	**%**	**p**
Male gender	87.88	75.00	0.17
Hypertension	78.79	80.56	0.85
Current smokers	0	13.89	0.03*
Prior PCI	78.79	80.56	0.86
Prior CABG	33.33	47.22	0.24
Heart failure	9.09	5.56	0.57
Acute myocardial infarction	81.82	91.67	0.22
Statins	81.92	94.44	0.10
Beta-blockers	84.85	88.89	0.61
Aspirin	90.91	94.44	0.57
ACEI-ARA II	66.7	63.89	0.39

Variables are expressed, unless otherwise stated, as mean (standard deviation). * p<0.05; AC: Active control. M: meditation. BMI: Body mass index. PWV: Pulse wave velocity. CBP: Central blood pressure. LDL-C: Low-density lipoprotein cholesterol. HDL-C: High-density lipoprotein cholesterol. us-CRP: Ultrasensitive C-reactive protein. PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass graft surgery; ACEI-ARA II: Angiotensin-converting enzyme inhibitors-Angiotensin-receptor antagonists.

Table 1. Baseline population characteristics

Continuous variables	AC (n=35) Δ, mean (SD)	M (n=35) Δ, mean (SD)	p
PWV, m/s	0.51 (1.40)	0.19 (1.53)	0.37
CBP, mmHg	5.,15 (20)	-3.07 (32)	0.09
Systolic BP, mmHg	4.84 (11.7)	1.52 (18.4)	0.39
Diastolic BP, mmHg	2.92 (9.56)	0.20 (10.0)	0.26
us-CRP, mg/L	1.17 (2.90)	-0.69 (0.89)	0.02*
SF-36, score	0.79 (7.58)	5.40 (9.69)	0.03*

*p<0.05.AC: Active control. M: meditation. SD: Standard deviation. PWV: Pulse wave velocity. CBP: Central blood pressure. BP: Blood pressure. us-CRP: C-reactive protein. SF-36: SF-36 Health Survey Questionnaire.

Table 2. Comparison of study end points

One of the hypotheses to explain us-CRP reduction is that M, through stress reduction, could modulate the level of neurohumoral activity and the associated sympathetic tone, acting on inflammatory parameters related to cardiovascular risk. (25-27)

Notably, APP intervention was not associated to a significant reduction in BP, a frequent finding in the literature exploring the effect of M in the cardiovascu-

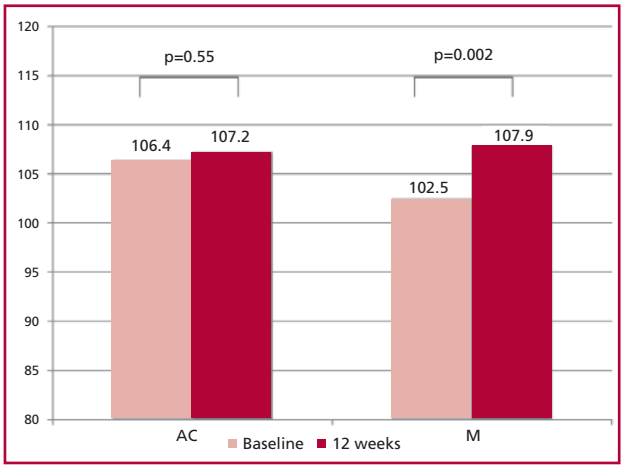

Fig. 2. Quality of life assessed by the SF-36 health survey questionnaire. AC: Active control. M: Meditation

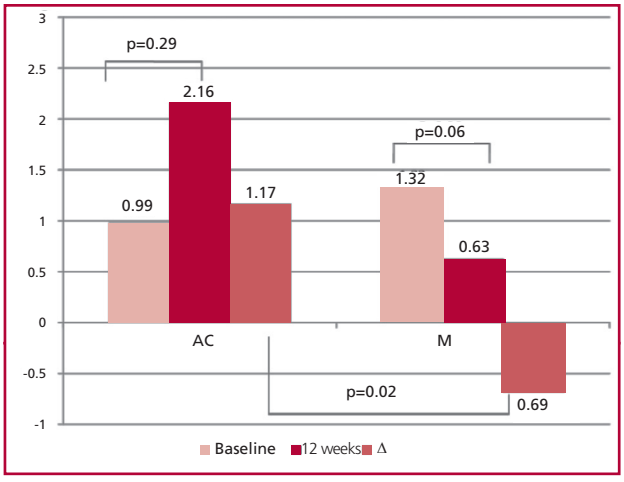

Fig. 3. Comparison of ultrasensitive C reactive protein in both groups. AC: Active control. M: Meditation.

lar context, particularly in TM publications. We believe that the characteristics of our population, with 100% of patients presenting with previous cardiovascular disease, elevated drug use (more than 80% were receiving beta-blockers, nearly 65% ACEI or ARAII agents and more than 90% statins or aspirin) and very low levels of total cholesterol and LDL-cholesterol, may have played a role in the scarce variation of this parameter, since studies evidencing MT-associated BP reduction mainly included patients without prior cardiovascular disease and lower use of cardiovascular drugs. Probably, the patients included in our study, with optimal standards of care and pharmacological regimen, had less margin to additionally improve BP. (28)

Regarding CBP, which in addition to its association with cardiovascular mortality (14) has been recently identified as a more stringent indicator of antihypertensive therapy, (29) it was significantly reduced in the M group (p=0.09)

As the intervention required training in a specific practice which the patients had to keep for 12 weeks, we decided to evaluate treatment adherence through telephone contact at prespecified intervals. Adherence above 75% was similar in both groups and was considered adequate.

Different publications in the international literature have evaluated the effect of meditation-based programs on clinical events. A study by Blumenthal et al. (30) reported that patients randomized to M had lower recurrence of coronary events at 5 years than those assigned to conventional treatment. Data from three randomized studies evaluating the impact of M on "hard" events reported between 30% and 48% relative risk reduction for overall mortality, cardiovascular death and infarction in patients assigned to an intervention group versus those receiving conventional care or education, as in our study. (31, 33)

LIMITATIONS

The main limitation of the study is its relatively small size. Moreover, the sample might also have low power to yield significant differences in patient baseline characteristics, considering that some variables (statin use, BP, CBP, male gender, infarction or prior surgery) might reach statistical significance with a larger sample size. Also, other confounders might affect the comparison between interventions; for example, the M program required a 70 Km trip to a natural environment that could have created different expectations than in those attending healthcare educational workshops. On the other hand, the degree of participant belief or confidence in the M technique might help or not the intervention placebo effect. Finally, the reproducibility of the M technique could be a limitation for routine use of this intervention.

CONCLUSIONS

A meditation program did not significantly modify PWV at 12 weeks in patients with previous cardiovascular disease. However, patients assigned to this intervention improved their quality of life and significantly reduced us-CRP levels. The incorporation of a simple practice, able to optimize parameters associated with the risk of new clinical events, could represent an alternative strategy to be recommended in patients with established cardiovascular disease. Further studies are necessary to confirm these findings, explore the mechanisms involved in this improvement and correct the limitations of this work.

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Conflicts of interest

The authors received partial financial support to perform the study from Alkymia Global in charge of the meditation program.

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