How to decrease cardiovascular risk factors in people with multiple sclerosis

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KEYWORDS
Multiple sclerosis; Cardiovascular diseases; Pulse pressure; Aerobic activity; Health education

Abstract

Background: There is an increased cardiovascular risk in people with multiple sclerosis (PwMS), which is associated with an increased risk of disease progression.

Objectives: To analyse the Cardiovascular Risk (CVR) of the sample in relation to Blood Pressure (BP) and to evaluate the effects of a combined health education and aerobic activity programme on Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Pulse Pressure (PP) Body Mass Index (BMI).

To quantify adherence to treatment.

Method: Closed clinical trial performed at Mas Sabater Day Hospital (Multiple Sclerosis Foundation).

The treatment group (TG) participated in an individualised 2-day/week 12-week progressive aerobic training programme and attended a health education programme to encourage healthy habits. The control group (CG) received routine care.

Results: Twenty-two PwMS were analysed (n = 22). The initial CVR of the sample was PP 47.23 (10.019) mmHg, SBP 121.91 (17.73) mmHg and DBP 74.68 (10.01) mmHg.

The TG decreased their SBP values with an average of 3.27 mmHg, the CG increased them by an average of 17.00 mmHg. In the CG, the PP increased an average of 11.91 mmHg, while in the GT it decreased 3.18 mmHg. The BMI of the GC increased 0.35 points, while in the GT it decreased 0.21.

Conclusions: Aerobic training combined with a health education programme decreases CVR in PwMS. Control of vascular comorbidities should be part of the treatment of MS.

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PALABRAS CLAVE
Esclerosis múltiple; Enfermedad cardiovascular; Presión de pulso; Actividad aeróbica; Educación sanitaria

Cómo disminuir factores de riesgo cardiovascular en personas con esclerosis múltiple

Resumen

Introducción: Existe un mayor riesgo cardiovascular (RCV) en personas con esclerosis múltiple (PcEM) que se asocia a un mayor riesgo de progresión de la enfermedad.

Objetivos: Analizar el RCV de la muestra en relación con la presión arterial (PA) y valorar los efectos de un programa combinado de educación para la salud y actividad aeróbica sobre los valores de PA sistólica (PAS), diastólica (PAD), presión de pulso (PP) e índice de masa corporal (IMC).

Cuantificar la adhesión al tratamiento.

Método: Ensayo clínico controlado realizado en el Hospital de Día Mas Sabater de la Fundación Esclerosis Múltiple.

El grupo tratamiento (GT) participó en un programa de entrenamiento aeróbico progresivo individualizado 2 días/semana 12 semanas complementado con un programa de educación sanitaria para la promoción de hábitos saludables. El grupo control (GC) realizó su actividad habitual.

Resultados: Se analizó una muestra de 22 PcEM. El RCV inicial fue de PP 47,23 (10,01) mmHg, PAS de 121,91 (17,73) mmHg y PAD de 74,68 (10,01) mmHg.

El GT disminuyó sus valores de PAS con una media de 3,27 mmHg y el GC los incrementó una media de 17,00 mmHg. En el GC la PP aumentó una media de 11,91 mmHg, mientras que en el GT disminuyó 3,18 mmHg. En relación con el IMC, el GC lo aumentó 0,35 puntos mientras que el GT lo disminuyó 0,21.

Conclusiones: El entrenamiento aeróbico combinado con un programa de educación sanitaria disminuye el RCV en pcEM. El control de las comorbilidades vasculares debe formar parte del tratamiento de la EM.

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Introduction

Multiple sclerosis (MS) is a degenerative disease that affects the central nervous system. It is characterised by inflammatory lesions that result in a loss of myelin and axonal damage. These lesions cause a great many primary motor, sensory and cognitive symptoms. The disease course of between 80% and 90% of persons with MS (PwMS) is relapsing-remitting, characterised by attacks followed by a partial or total recovery. After a period from 10 to 15 years the disease enters a secondary progressive course where the level of disability increases. The disease is progressive in between 10% and 20% of PwMS.1

MS is the second cause of disability in young adults. The latest studies indicate a rate in Spain of 125 cases per 100,000 inhabitants,4 and a growing trend has been confirmed over recent decades.

In addition to the diseases’ primary symptoms, several studies report health conditions that are more common in people diagnosed with MS.3,4 Depression, anxiety, high blood pressure (HPB), hypercholesterolaemia and chronic lung disease are the 5 prevailing non-autoimmune conditions.3,4

The studies published to date are inconclusive, but it seems that PwMS have a risk of developing cardiovascular disease. In the progressive course of the disease venous thromboembolic disorders are more common, probably associated with immobility.4,5

Marrie et al., in their study published in 2010, found that patients with MS with a vascular comorbidity during the course of their disease progressed to a score of 6 on the Expanded Disability Status Scale (EDSS) on average 6 years earlier than MS patients who had never experienced a vascular comorbidity.1 Therefore, vascular disease is associated with a significantly greater risk of the disability of PwMS progressing.

Most cardiovascular diseases can be prevented by tackling the risk factors that cause them, such as smoking, poor diet, physical inactivity and alcohol consumption.6,7 Early detection and treatment that includes increased physical activity and promoting healthy habits are essential to prevent complications in the general population.7 In MS, establishing, defining and measuring the comorbidity will improve the management of the patient. In these cases, acting on the most common comorbidities delays progression of disability, which is linked to the number of concurrent processes and habits.

Despite the clinical course, which is often unpredictable, well-designed exercise programmes can increase cardio respiratory capacity, muscle strength and mobility and therefore provide benefits in terms of quality of life while reducing the risk of secondary disorders.

It is important to stress that controlled physical activity is not associated with a greater risk of relapse and the risk of adverse events is no greater than that of the healthy population.8
There is also scientific evidence of the effects of physical activity on other symptoms that affect PwMS. It is known that it could be potential treatment to prevent or reduce symptoms of depression,\textsuperscript{9} and can be a modulator of beneficial neuronal growth factors due to the complex interventions of certain hormones, cytokines and nerve factors that could have a favourable influence on immune variables.\textsuperscript{10,11}

Numerous epidemiological studies demonstrate a correlation between increased pulse pressure (PP) and cardiovascular morbidity and mortality. PP is defined as the difference between systolic blood pressure (SBP) and diastolic blood pressure (DBP); it is expressed in mmHg and considered an indicator of arterial compliance. It is a marker of cardiovascular events in both normotensive and hypertensive populations, especially when due to increased SBP and reduced DBP.\textsuperscript{12} Benetos et al. observed that people whose PP levels were greater than or equal to 55 mmHg had an increased relative cardiovascular risk of 44\% compared to the group with lower PP levels.\textsuperscript{13} In 1999, Millar et al. found that PP was a stronger predictor of coronary events than SBP, and the SHEP study established an association between increased PP and cerebrovascular events.\textsuperscript{14} Framingham’s study, published in 1999, confirmed that increased SBP, DBP and PP were associated with a greater cardiovascular risk, PP being the variable with the highest correlation of the three.\textsuperscript{15}

At present there are no practical cut-off levels that separate normality from abnormality in relation to PP. With hypertensive subjects, the HBP management guidelines (2007) place the level at 50–55 mmHg.\textsuperscript{16} In 2013, the European directive increased this threshold to 60 mmHg with no obvious justification.\textsuperscript{17}

BMI is also considered another modifiable risk factor for cardiovascular disease. At present, excess weight and obesity are considered as important as other traditional risk factors (diabetes, dyslipidaemia, HBP, etc.) associated with coronary disease. They have many cardiovascular repercussions, either directly or through other risk factors. Two thirds of people with cardiovascular disease are overweight.\textsuperscript{18} The risk of a coronary event is 3 times greater in people with a BMI > 29 kg/m\(^2\) compared to those whose BMI < 21.\textsuperscript{19}

The general aim of this study was to evaluate the effects of a combined programme of health education and aerobic exercise on BP, PP and BMI. Adherence to the treatment prescribed was studied.

Method

Controlled clinical trial

Service users with a diagnosis of MS, an EDSS score lower than 6, and with no medical contraindication to aerobic exercise were selected from the census of the Mas Sabater day hospital of the FEM (Multiple Sclerosis Federation). The people who agreed to participate and who met the described inclusion criteria were allocated at random to either the CG or the TG. The exclusion criteria were contraindication to physical exercise and failing to meet the inclusion criteria.

Each participant was initially assessed using the scales detailed below and subsequently given their treatment.

In addition to the usual treatment, the GT were given an aerobic exercise regime based on walking, twice a week for 30 min using the Healthy Routes of the municipalities of Catalonia participating in the Pla d’Activitat Fisica, Esport i Salut (PAFES) (Physical Activity, Sport and Health Plan) of the Ministry of Health and the Sports Ministry, and 4 health education sessions to encourage healthy habits and lifestyle. These sessions included recommendations for a healthy diet, rest and physical activity. The dietary recommendations included information on the appropriate nutrients for the expected physical activity and how to distribute them throughout the day.

The treatment lasted for 12 weeks (October 2015 to December 2015) and was directed and supervised by healthcare professionals (physiotherapist and nurse), who were specialists in the treatment of people with MS. The sessions that could not be performed in the open air due to the weather were replaced by an alternative aerobic activity (static cycle ergometer) in the Mas Sabater day hospital.

The CG followed their routine prescribed treatment, they underwent no assessment and it was confirmed that they had made no changes to their habits or lifestyle.

All the participants were reassessed on completion of the intervention.

The project was assessed and approved by the research ethics committee of the University hospital, approval reference 15-09-24/9aclaoa01.

The data obtained were analysed using IBM, SPSS (Statistical Package for Social Sciences) version 22. Standard deviation (SD) was used for the descriptive analysis of the quantitative variables. The qualitative variables were presented using relative and absolute frequencies. Finally, the Mann–Whitney U test was used for independent variables. Means (SD) were used to describe the continuous data.

Variables studied

- Type of MS. Classified by form of progression: primary progressive MS (PPMS), relapsing-remitting multiple sclerosis (RRMS) and secondary progressive MS (SPMS).
- EDSS. Kurtzke’s expanded disability status scale score.\textsuperscript{19} The EDSS is a method for quantifying disability in MS; it measures the level of involvement of 8 functional systems: pyramidal, cerebellar, brainstem, sensory, bladder, bowel, visual and mental functions.
- Year of diagnosis. This means the year when the condition was diagnosed, not of the onset of the first symptoms.
- BP. Measured with the patient seated, feet on the ground and without crossing their arms. The arm should be support to ensure that the forearm is at the level of the heart. The sphygmomanometer is placed on the forearm; the lowest edge of the sleeve should be one finger above the fold of the elbow. The sleeve should be rapidly inflated, and then the sleeve valve gently opened so that the pressure descends slowly.
- Pulse pressure. Defined as the difference between SBP and DBP and expressed in mmHg. Considered a cardiovascular risk factor.
- Weight. Measured in kilograms on floor scales for ambulant subjects.
Table 1  Initial values of CVR.

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>p Value</th>
<th>Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial SPB</td>
<td>Control</td>
<td>112.00</td>
<td>11.31</td>
<td>.013</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>131.82</td>
<td>17.78</td>
<td></td>
</tr>
<tr>
<td>Initial DPB</td>
<td>Control</td>
<td>70.55</td>
<td>6.51</td>
<td>.210</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>78.82</td>
<td>12.51</td>
<td></td>
</tr>
<tr>
<td>Initial pulse</td>
<td>Control</td>
<td>41.45</td>
<td>6.87</td>
<td>.002</td>
</tr>
<tr>
<td>pressure</td>
<td>Treatment</td>
<td>53.00</td>
<td>9.49</td>
<td></td>
</tr>
</tbody>
</table>

- Height. Measured in centimetres with a vertical height rod.
- BMI. Calculated by dividing the participant’s weight by their height squared.

BMI classification:
- <18.5.
- 18.5–24.9 normal.
- 25–29.9 overweight.
- 30–34.9 type I obesity.
- 35–39.9 type II obesity.
- 40 type III obesity.

Results

Twenty-six people from the HD census met the inclusion and exclusion criteria. Initially the project consisted of 13 people in the CG and 13 in the TG. Two withdrew from the TG, one because of a debilitating attack that prevented them from walking and the other due to a fracture of the fourth and fifth metatarsal bones of the left foot that required rest. One of the CG participants was excluded because they had started a water activity, and one of the TG participants due to a change in their antihypertensive drug regimen.

Twenty-two MS patients were studied of a mean age (SD) of 46.50 (8.3) years and EDSS between 2.0 and 6.0 points. Seventy-seven point three percent of the sample was female, and 22.70% male. In terms of the form of progression of the disease, 81.80% had RRMS, 18.20% SPMS and .00% PPMS.

The initial cardiovascular risk factors of the sample were measured through mean PP, SBP and DBP readings: PP 47.23 (10.01) mmHg, SBP 121.91 (17.73) mmHg and DBP 74.68 (10.01) mmHg.

The initial values according to the allocated group are shown in Table 1.

After the health education and training programme, the TG reduced their SBP levels, while they increased in the CG (p = .023), the same occurred with PP (p = .04). The changes in DBP were not statistically significant (p = .270) (Fig. 1).

Figs. 2 and 3 show us the results obtained when classifying the data according to group.

We can see that at the start, 50% of the sample had a normal BMI compared to 50% who did not; 27.3% were overweight, 13.6% were grade 1 obese, 4.5% grade 2 obese and 4.5% grade 3 obese.

The BMI reduced in the TG with statistically significant levels (p = .040). The CG increased their BMI by a mean .35 points, whereas that of the GT reduced by .21.

Ninety-eight point twenty percent of the scheduled sessions were completed.

Discussion

Published studies on comorbidity highlight HBP as one of the 5 most prevalent non-autoimmune diseases in MS,9 that there is a risk of cardiovascular disease in people with the condition and that vascular comorbidity is associated with a significantly higher risk of progression of disability.1,21
HBP, excess weight/obesity, physical inactivity, smoking, hypercholesterolaemia, diabetes mellitus and poor dietary habits are considered cardiovascular risk factors and responsible for approximately 80% of coronary heart and cerebrovascular disease. The Fourth Joint Task Force European guidelines on cardiovascular prevention and its Spanish version recommend that these factors should be monitored. BP, BMI and other biochemical parameters are useful in determining the risk of cardiovascular events in the general population. In the case of PP, our review of the literature revealed that there is no consensus as to what is considered a normal PP, and because the stratification guidelines refer to hypertensive patients or the elderly we did not categorise the risk in our analysis, in the understanding that both an increase in PP and an increase in SBP are independent variables of cardiovascular risk, as the reviewed literature shows.

As Zhao et al. confirm, determining brachial pulse pressure can help to identify patients at greater risk of mortality events and, therefore, help in timely therapeutic decision-making.

An inverse association has been demonstrated between regular exercise and the risk of coronary disease, cardiac events and death. Exercise improves lipid levels and blood sugar control, reduces or prevents HBP, obesity and stress, improves physical fitness and increases functional capacity, increasing years of independent living and improving quality of life. In our sample we saw that aerobic exercise accompanied by a health education programme had beneficial effects on the variables studied.

There is clear consensus that lifestyle strategies play a fundamental role in the prevention, management and reduction of cardiovascular disease and its risk factors. In the general population, these strategies have been widely studied and implemented; the Government of Catalonia’s Health Department, in line with the World Health Organisation’s Global Strategy on Diet, Physical Activity and Health, have deployed the integral plan for health promotion through physical activity and health eating. The purpose of this programme is to raise awareness among the population on the prevention of health risks, to implement information and educational activities focussing on lifestyle and to encourage healthy habits. Pilot initiatives exist for specific populations such as that described in this study.

We can see that in the case of MS there is increasing evidence of the benefits of exercise, but this population is generally inactive and sedentary. Studies that directly compare physical activity patterns in patients with MS, patients without MS and patients with other chronic diseases indicate that patients with MS might be at the lowest end of the spectrum in terms of taking physical exercise.

Education is one of the commonest and most useful activities to ensure therapeutic compliance. The role of health professionals in promoting and recommending physical activity is essential to ensure good adherence to exercising, increasing motivation levels and involving the patient actively in their therapeutic plan. Smith et al. performed a study on people with MS and found that the motivational interview had an effect on adherence to the exercise programme. Rejeski and Kenney recommend, in addition to educating the patient, that social influence should be maximised and interaction between participants encouraged to ensure continuity of the activity and to prevent dropouts. In our case, the fact that the activity took place in groups, in the open air and combined with a health education programme resulted in an adherence level of 98.2%.

**Conclusions**

The results show that aerobic training along with a health education programme reduced SBP, PP and BMI in our sample.

Because the published literature shows that HBP is one of the most prevalent comorbidities in MS and confirms that cardiovascular comorbidity is associated with a poorer outcome of the disease, it is essential to establish risk. In the context of our social and health department specialising in neuro-rehabilitation at the day hospital, establishing parameters such as BP, PP and BMI can be an ideal way of establishing risk, since we have no tools to assess biochemical parameters.

It is also important to find ways of ensuring continuity of physical activity and this was achieved through educating the patients. The role of health professionals in promoting and advising physical exercise is essential to achieve adherence, increasing patients’ motivation levels and making them responsible for and actively involved in their therapeutic plan. Different authors recommend that social influence should be maximised in addition to educating patients, and they should be encouraged to interact to ensure continuity and prevent dropouts. Here, the MS specialist nurse plays an essential role.

The literature recommends promoting healthy habits and lifestyles. A healthy diet and regular exercise have been widely demonstrated to be effective in cardiovascular prevention. Prevention is, therefore, one of the most important tools.

We consider controlling vascular comorbidities a complementary route in the treatment of MS. Acting on comorbidities delays progression of the disease, which is linked to the number of concurrent processes and habits.

Further studies are required to determine the long-term effects on the same variables, since on disaggregating the BMI parameters we observed a reduction in weight levels.
that was not statistically significant, probably due to the short duration of the study and increased height levels, probably due to postural correction.

Conflict of interests

The authors have no conflict of interest to declare.

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