

## Research Submission

# A Study to Evaluate the Feasibility of an Aerobic Exercise Program in Patients With Migraine

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**Objectives.**—The aim of this study was to develop and evaluate an exercise program to improve maximum oxygen uptake ( $VO_{2\text{ max}}$ ) in untrained patients with migraine without making their migraines worse.

**Patients and methods.**—Twenty-six patients were studied at a headache clinic in Sweden. The exercise program, based on indoor cycling, was performed 3 times per week during 12 weeks.  $VO_{2\text{ max}}$ , migraine status, side effects, and quality of life were evaluated.

**Results.**— $VO_{2\text{ max}}$  increased from 32.9 mL/kg/minute to 36.2 mL/kg/minute ( $P = .044$ ). Quality of life increased and significant improvements in migraine status (attack frequency, symptom intensity, and intake of medicine) were seen. During the 12 weeks of exercise, on one occasion one patient had a migraine attack, which started immediately after training. No other side effects were reported.

**Conclusions.**—The evaluated exercise program was well tolerated by the patients and improved their  $VO_{2\text{ max}}$  with no deterioration of migraine status.

**Key words:** migraine, exercise, maximum oxygen uptake, indoor cycling

**Abbreviations:** MSQoL Migraine Specific Quality of Life questionnaire, RPE scale Borg's Rate of Perceived Exertion scale,  $VO_{2\text{ max}}$  maximal oxygen uptake

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Physical activity is usually recommended in health promotion and disease prevention.<sup>1</sup> For people with migraine, too, exercise is often suggested.<sup>2-5</sup> One difficulty for patients with migraine in doing exercise is that, in the short term, the exercise can provoke attacks. In a recent study, 22% mentioned exercise as a migraine trigger.<sup>6</sup> This is one of the reasons some

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patients with migraine avoid exercise. These facts are also supported by a study showing that patients with headache had less aerobic endurance and flexibility than healthy control subjects.<sup>7</sup>

There are no guidelines in the literature regarding how patients with migraine should be instructed to exercise. For that reason guidelines for frequency, intensity, and duration of training are often those referred to for the general health promotion.<sup>8-10</sup> In the published research, submaximal aerobic exercise with intensity between 50% and 85% of maximal heart rate has been used. The training frequency in those studies were 3 times a week and the duration ranged from 30 to 60 minutes.<sup>11-14</sup> No studies have been made to find the optimal "dose" for exercise in patients with

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migraine, nor are negative side effects documented and compared with beneficial effects.<sup>2</sup>

Owing to the shortage of studies of exercise and migraine and the difficulties associated with exercise for migraine patients, it is important to define methods for exercise that are safe and do not increase attack frequency. The aim of this study was therefore to develop and evaluate a method of exercise for untrained patients with migraine, which could safely improve exercise capacity without making their migraines worse.

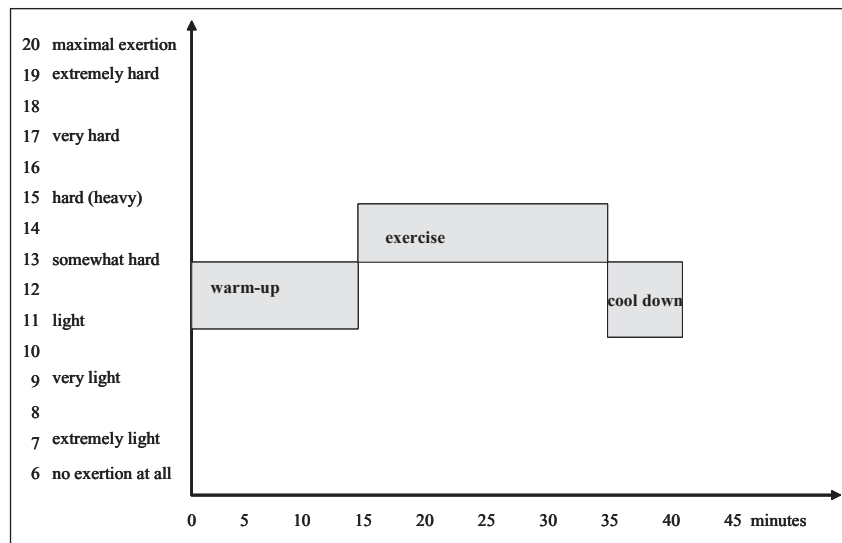
## METHODS

**Participants.**—Twenty-six untrained patients with migraine were recruited and studied at a tertiary headache clinic in Sweden. “Untrained” was defined as not having exercised regularly more than once per week during the 12 weeks prior to the study. The Ethics Committee of Göteborg University approved the protocol of the study. Written informed consent was obtained from all patients. Participants were recruited via newspaper advertisements and among patients already attending the clinic. All patients were examined by a neurologist and the diagnosis was given according to the criteria of the International Headache Society (International Classification of Headache Disorders, 2nd edition). Patients fulfilling

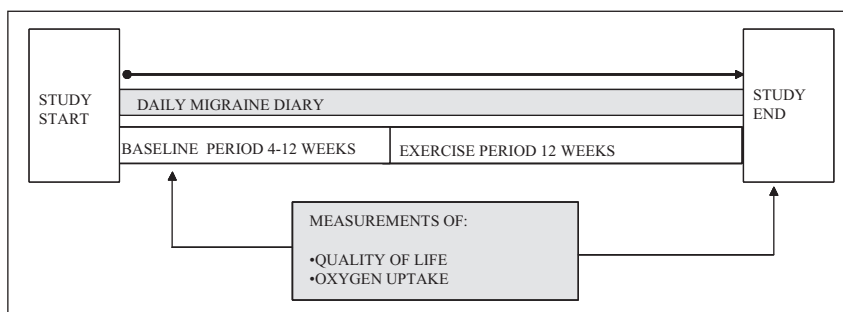
inclusion criteria and not fulfilling exclusion criteria for the study were invited by the neurologist to participate in the study.

Inclusion criteria were: age between 18 and 65, migraine with or without aura with a frequency of 2-8 attacks per month, debut of migraine attacks at least one year before study inclusion and before the age of 50. Exclusion criteria were: interval headache not distinguishable from migraine, patients who had exercised regularly more than once per week during 12 weeks prior to the study, pregnancy, breast feeding, use of daily migraine prophylaxis 12 weeks prior to the study, inability to understand Swedish, antipsychotic or antidepressive medications 12 weeks prior to the study, abuse of drugs or alcohol.

**Exercise Program.**—The exercise program was based on indoor cycling. Borg’s Rate of Perceived Exertion scale (RPE scale, 6-20) was used to set the training intensity.<sup>15</sup> The RPE scale is described in Figure 1. Each training session included a 15-minute warm-up period (intensity: RPE scale, 11-13), followed by a 20-minute exercise period (RPE scale, 14-16) and a 5-minute cool-down period (RPE scale, 11-13). During the training session music was included to make the program more pleasant. The patients trained with a physiotherapist 3 times a week for 12 weeks. The frequency and intensity of



**Fig 1.**—The exercise program. Borg’s Rate of Perceived Exertion scale (RPE scale, 6-20) was used to set the training intensity. Each training session included a 15-minute warm-up period (intensity: RPE scale, 11-13), followed by a 20-minute exercise period (RPE scale, 14-16) and a five-minute cool-down period (RPE scale, 11-13).



**Fig 2.—The study procedure. The study included a baseline period (4-12 weeks) followed by a treatment (exercise) period (12 weeks). Migraine diaries regarding frequency and intensity of pain and doses of medicine were kept throughout the whole study. Quality of life and oxygen uptake were measured on 2 occasions, during the baseline period and directly after the treatment period.**

training were based on recommendations for increasing maximal oxygen uptake ( $VO_{2max}$ ) from the American College of Sports Medicine (ACSM)<sup>9</sup> and the authors' clinical experience of migraine and exercise. All patients had the opportunity to discuss the training with the physiotherapist *ad hoc*. In case of absence, the patients were instructed to train at home or at a local gym. All forms of continuous aerobic exercise (eg, cycling, jogging, Nordic walking or swimming) were accepted. They were instructed to use the same intensity and duration as in the exercise program at the clinic. Compliance with treatment was defined as training once a week at the clinic and a minimum total of two-thirds of the total number of training sessions. The patients were instructed to keep a diary regarding exercise during the 12 weeks.

**Assessments.**— $VO_{2max}$ , migraine frequency and intensity, intake of headache medication, side effects, and quality of life were evaluated.

**Maximal Oxygen Uptake.**—The  $VO_{2max}$  is a measure of the maximum amount of oxygen that can be utilized during exercise (measured in milliliters of oxygen per kilogram of body mass per minute). The ability to utilize oxygen increases with the level of fitness. Therefore, the  $VO_{2max}$  is often used to evaluate the aerobic capacity.<sup>16</sup> Before and directly after the treatment period, the estimated  $VO_{2max}$  was measured using Åstrand's submaximal bicycle test.<sup>17</sup> This test has been shown to be reliable and valid.<sup>18,19</sup> The tests were performed by an experienced physiotherapist who was not involved in the treatment. The test was performed on a Monark 828E ergometer cycle

(Monark AB, Varberg, Sweden), and the pulse rate was assessed using a Polar FS1 pulse watch (Polar, Guangzhou, China).

**Migraine Status.**—The patients were instructed to keep migraine diaries regarding migraine attacks, days with migraine, daily amount of headache medication used (doses of tablets, injections, nasal sprays, and suppositories), and the daily average migraine pain during the baseline period (4-12 weeks) and during the treatment period (12 weeks). The diary was based on the visual analog scale, which consists of a 100-mm straight line with "no pain" as one endpoint and "worst imaginable pain" as the other.<sup>20</sup>

**Side Effects.**—The patients were instructed to report side effects in their migraine diaries.

**Quality of Life.**—Quality of life was assessed using the Migraine Specific Quality of Life questionnaire (MSQoL). It consists of 20 items, each of which is rated using a response scale with 4 categories (1 = very much and 4 = not at all). The data were then standardized to a range of values from 0 to 100, where 0 represents worst health status and 100 represents best health status. MSQoL has good reliability and validity.<sup>21,22</sup> The questionnaire was filled in before and after the treatment period.

**Procedure.**—The study procedure is described in Figure 2. All patients were allowed to contact the physiotherapist or the neurologist for questions via phone, e-mail or by appointment during the study. No restrictions were placed on the use of concomitant acute medication.

**Statistics.**—Data are expressed as mean values  $\pm 1$  standard deviation and median with interquartile

range. The primary measure was  $VO_{2max}$ . Secondary measures were number of migraine attacks per month, days with migraine per month, mean headache intensity, amount of headache medication used, and MSQoL. The values from baseline regarding attacks, days with migraine, mean headache intensity, and amount of headache medication used were compared with the whole treatment period and with the last month of treatment. The results in  $VO_{2max}$  and MSQoL during the baseline period were compared with the assessment after the treatment period. Wilcoxon signed rank test was used for comparisons. A value of  $P < .05$  was considered statistically significant. All analyses were performed using the Statistical Package for Social Sciences software program, version 13 for Microsoft Windows.

## RESULTS

Out of the 26 patients, 20 completed the treatment period. The reasons for dropout/withdrawal were lack of time ( $n = 3$ ) and noncompliance with treatment ( $n = 3$ ).

All of the 20 patients performed both  $VO_{2max}$  tests. Nineteen returned their migraine diaries and 18 returned the MSQoL questionnaires.

The 20 patients (17 women) were between 36 and 63 years old (median age 49 years). Seven had a migraine diagnosis without aura, one had migraine with aura, and 11 had migraine with and without aura. The median number of years since the debut of migraine was 32 (range 13-50 years). The patients are described in Figure 3.

**Oxygen Uptake.**—After the treatment period,  $VO_{2max}$  max increased significantly as compared with baseline, 32.9 (10) mL/kg/minute vs 36.2 (8) mL/kg/minute ( $P = .044$ ) (Table 1).

**Migraine Status.**—There was no deterioration in migraine status concerning any of the variables evaluated. On the contrary, during the last month of treatment there was a significant decrease in both the number of migraine attacks and the number of days with migraine per month, mean headache intensity, and amount of headache medication used as compared with baseline (Fig. 4, Table 1).

**Side Effects.**—None of the patients reported side effects in the diaries. In conjunction with the training

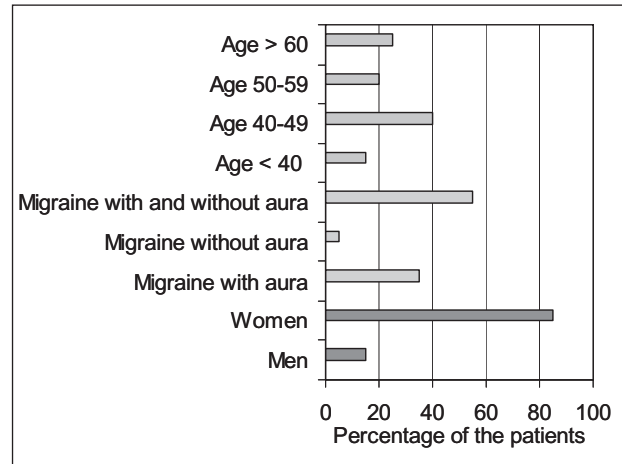


Fig 3.—Demographic profiles of patients.

sessions, on one occasion one of the patients had a migraine attack (migraine with aura), which started immediately after training.

**Quality of Life.**—There was a significant increase in MSQoL after treatment compared with baseline (Table 1).

## DISCUSSION

To our knowledge, this is the first detailed description and evaluation of a method for exercise to improve oxygen uptake in patients with migraine. In the present study a small convenient sample of migraineurs were studied before, during, and after an aerobic exercise intervention. We found that they tolerated it well with no reported increase in migraine and in fact some improvement in reported migraine status and other things such as quality of life. We have demonstrated how a group of untrained patients with severe migraine increased their exercise capacity without inducing a concomitant deterioration of their migraines or negative side.

An important part of our study was to see that the method was well tolerated and did not make the migraines worse. We therefore chose to evaluate migraine attacks, days with migraine, daily amount of headache medication used (doses of tablets, injections, nasal sprays, and suppositories), the daily average migraine pain, side effects of treatment, and quality of life in order to cover as many aspects as possible of the burden of migraine.<sup>23,24</sup> None of these

**Table 1.—Results from Migraine Specific Quality of Life Questionnaire (MSQoL), Maximal Oxygen (VO<sub>2max</sub>), and Migraine Status**

	MSQoL (points)†	VO <sub>2max</sub> (mL/kg/minute)	Migraine attacks/month	Days with migraine	Intensity of pain (VAS in mm)†	Doses of acute medicine
Baseline	58 (37)	32.9 (9.8)	4.7 (2.0)	7.5 (3.6)	57 (36)	7.6 (3.7)
Treatment			3.9 (1.6)	6.4 (3.3)	42 (34)	6.6 (2.5)
			ns	ns	ns	ns
Last month of treatment			3.6 (1.9) <i>P</i> = .027	5.4 (3.6) <i>P</i> < .01	47 (33) <i>P</i> = .019	5.8 (3.7) <i>P</i> = .024
After treatment	65 (25) <i>P</i> < .01	36.2 (8.1) <i>P</i> = .044				

Mean values with standard deviations (in parentheses).

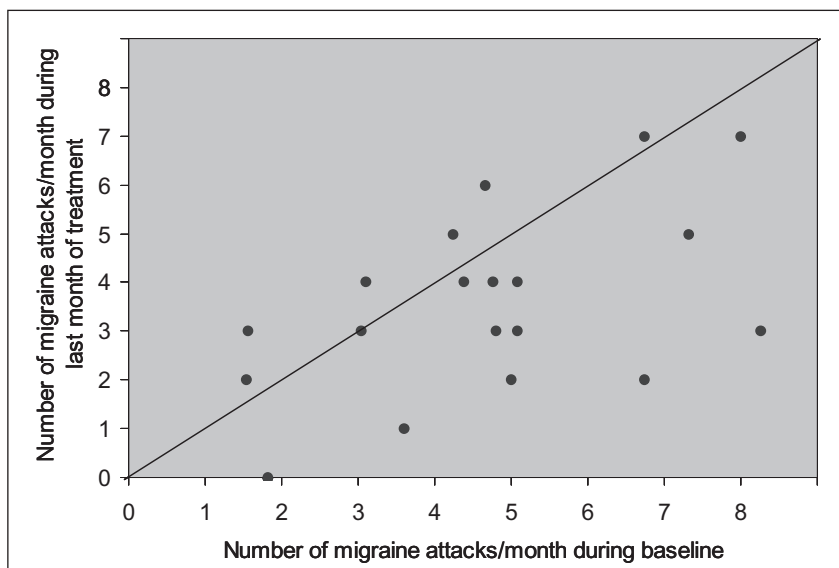
†Median value with interquartile range (given within parentheses) significant change from baseline.

ns = nonsignificant; VAS = visual analog scale.

parameters were deteriorated in our study. The positive results reported in migraine status and quality of life are encouraging but inconclusive, since this was not a blinded study and there was no control group.

In earlier reports on migraine and exercise, side effects are not discussed.<sup>2</sup> Exercise has, however, been found to cause complications.<sup>25,26</sup> Specific injuries related to cycling are suggested to be caused by a combination of inadequate preparation, inappropriate equipment, poor technique, and overuse.<sup>27,28</sup> In order to avoid this, we found it important for the patients to be supervised by a physiotherapist.

The program was designed using general recommendations for increasing VO<sub>2max</sub>, earlier reports on migraine and exercise, and the authors' clinical experience. To develop and maintain cardiorespiratory fitness, the ACSM recommends aerobic exercise 3-5 days a week, 20-60 minutes with an intensity of 55/65-90% of maximum heart rate. The lower values are applicable for individuals who are quite unfit.<sup>9</sup> Converted to the RPE scale, this means 12-16.<sup>29</sup> Higher-intensity exercise is associated with greater cardiovascular risk<sup>30</sup> and orthopedic injury<sup>31</sup> and lower adherence to training.<sup>32,33</sup> We designed the



**Fig 4.—Number of migraine attacks/month at baseline as compared with last month of treatment. The majority of the patients had fewer migraine attacks during the last month of treatment than at baseline.**

exercise program based on these recommendations. An additional reason for choosing a moderate-intensity level was that it may be a contributing factor to avoid exercise-induced migraine.<sup>34,35</sup> Insufficient warm-up is reported to be a migraine trigger, and migraine attacks are suggested to be preventable by proper warm-up before exercise.<sup>36</sup> In the program we therefore used a 15-minute warm-up period estimated as light to somewhat hard, according to the RPE scale. We hypothesized that the intensity, duration, and frequency of exercise are more important than the type of exercise in this patient category. Therefore, we accepted different forms of continuous aerobic exercise apart from cycling, when the patients were absent from a training session at the clinic and exercised at home. We also found it important to establish a way of performing aerobic exercise that would be easy to use in settings other than at a specialist clinic. Hence, we chose the RPE scale instead of percentage of maximal heart rate, which is used in other studies to set the intensity level.<sup>12,13</sup> Owing to the relatively high migraine attack frequency in the patient group (up to 8 attacks/month), it was difficult for the patients to attend all the scheduled training sessions at the clinic. The protocol was therefore designed to make it possible to exercise at home, on days when the patients were free from migraine. Another reason for allowing them to train at home was to reduce the experience of stress. To avoid exercise-induced migraine, it also seems reasonable to reduce other environmental trigger factors such as stress, as well as to consider proper sleep, good nutrition and hydration.<sup>37</sup> In our study we pointed out these facts before the baseline period began, and reminded the patients of them regularly during the study.

Six out of 26 patients did not finish the study. The reasons were: dropout during the baseline period owing to lack of time ( $n = 3$ ) and noncompliance with treatment ( $n = 3$ ). The patients defined as noncompliers with treatment exercised for less than two-thirds of the total number of training sessions. The reason given for this was also lack of time. As far as we know, none of the patients avoided the training sessions owing to deterioration of their migraines.

The test used for evaluation of maximal oxygen uptake, Åstrand's submaximal bicycle test, is a widely

used test. It has been validated in a study on Swedish men and women, where the predicted  $\text{VO}_{2\text{max}}$  based on Åstrand's submaximal method was compared with matched, direct measures of  $\text{VO}_{2\text{max}}$  during maximal work on a treadmill.<sup>19</sup> The reason for not choosing a maximal test was that it might be a less suitable option for patients with migraine, since vigorous physical exercise may trigger attacks. Another reason is that the Åstrand procedure is simple, without the need for sophisticated laboratory equipment.

One important question is whether or not the patients continue their exercise after the study period. Therefore, follow-up studies are important. Previous reports of studies on exercise interventions show poor long-term compliance.<sup>38</sup>

There are some important limitations that must be considered in the interpretation of the results. The study was based on a convenience sample of migraineurs and the generalizability of our findings is thus not clear. We cannot say with certainty that the selected group of respondents is representative of patients with migraine in the general population. Furthermore, patients who experience physical exercise as a trigger for their migraine attacks could have chosen not to enrol in the study. These factors make generalization of the results difficult. The results from our study are promising, but the fact that the study is uncontrolled makes it impossible to draw conclusions about the benefits in migraine status. The improvements reported in migraine status can be explained by placebo effects, regression to the mean or both. Whereas no randomized controlled studies of good quality yet have been performed on this topic,<sup>2</sup> well-designed studies of exercise in patients with migraine are imperative.

## CONCLUSIONS

In this study we have described and evaluated a method of exercise, which was well tolerated by the patients. The program, based on indoor cycling (continuous aerobic exercise), including warm-up and cool-down periods, is shown to improve maximal oxygen uptake without making the patients' migraines worse.

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