

Effectiveness of behavioural management on migraine in adult patients visiting family practice clinics: a randomized controlled trial

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Abstract

Objectives: To assess the effectiveness of behavioural management in the treatment of migraine among adult patients.

Methods: The randomised control trial was conducted from August 2011 to August 2012 at the Aga Khan University Hospital, Karachi, in which adult patients aged 18-65 years were recruited with diagnosis of migraine from five outpatient sites. The patients were randomised into 2 equal groups. The controls were given pharmacological treatment, while the cases were given a structured behavioural management and pharmacological treatment. Primary outcome was the change in frequency of migraine attacks. Secondary outcome included change in severity of migraine and effect on the quality of life. SPSS 19 was used for statistical analysis.

Results: Of the 90 subjects in the study, 72(80%) were female. A significant reduction in the average frequency of migraine attacks was observed from baseline up to 4 weeks ($p < 0.001$) but no difference in the mean migraine attacks was observed in the two groups ($p < 0.945$). In the average score of severity of pain, significant reduction was observed for time ($p < 0.001$) as well as for the intervention status ($p < 0.034$). There was no significant difference ($p < 0.450$) between treatment type and duration of migraine, but a significantly better quality of life ($p < 0.001$) was observed in the trial group compared to the controls.

Conclusion: There was significant decrease in frequency, severity and duration of migraine attacks in the trial group compared to the control group. The quality of life also showed improvement in the trial group.

Keywords: Migraine headaches, Deep breathing exercises, Behavioural management, Relaxation techniques. (JPMA 64: 900; 2014)

Introduction

World Health Organisation (WHO) ranks headache disorders amongst the ten most disabling conditions in the world. Globally, the percentages of the adult population with an active headache disorder are 46% for headache in general, 11% for migraine, 42% for tension type headache and 3% for chronic daily headache.¹ In another study, prevalence of current headache disorders (symptomatic at least once within the preceding year) among adults aged 18-65 years is 47% and nearly 1.7% to 4% of the world's adult population suffer headaches on 15 or more days every month.² International studies show that migraine affects approximately 18% of women and 6% of men worldwide.³ Unfortunately, headaches' morbidity has largely been unaddressed and under-recognised in the developing world.⁴ A study conducted in Karachi, Pakistan, on 255 patients (169 women and 86 men; aged 15-49 years) who attended the specialist headache clinic in the study period, Migraine was the most commonly diagnosed primary headache found in

206 (81%) patients. There were 68% women with a male-to-female ratio of almost 1:2.5 Migraine causes severe impairment in quality of life (QOL) both during and between attacks. QOL is defined by WHO as individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns during and between attacks.⁶ Migraine also increases absenteeism, reduces productivity at work, and is associated with increased healthcare costs. It causes bed rest in more than half (57%) of the affected people in the United States.⁷ A recent study published in Lancet showed migraine ranked 8th among the most disabling conditions out of 289⁸ with approximately 1.3% years lost due to disability (YLD).⁹ Patients presenting with migraine have been treated with pharmacological and non-pharmacological treatments. Nonetheless, the pharmacological treatments have certain risks such as side-effects and over-dose. Headache literature, dating as far back as 1960s, shows that patients have been treated with non-pharmacological interventions namely behavioural treatments, as alternative and adjunct therapy with reduction in headache frequencies.¹⁰ Different behavioural interventions are available including cognitive behavioural therapy and bio-

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behavioural training (i.e., biofeedback, relaxation training, and stress management). Studies comparing behavioural and prophylactic medication show equivalent results.¹¹⁻¹³ A meta-analysis of 39 studies concluded that relaxation training, electromyography biofeedback, thermal biofeedback with relaxation and cognitive behavioural therapy were all more effective with 32-49% reduction in headache frequency.¹⁴ Another meta-analysis which integrated results from 25 clinical trials evaluating the effectiveness of propranolol and 35 clinical trials evaluating the effectiveness of relaxation/biofeedback training yielded a 43% reduction in migraine headache activity in the average patient in both the groups.¹⁵ A meta-analysis of 55 biofeedback studies demonstrated big improvements in headache frequency and perceived self-effectiveness with effects stable up to 17 months of follow-up.¹⁶ Another study of long-term maintenance of reduction of symptoms achieved with pharmacological therapy (ergotamine) vs. non-pharmacological (relaxation and thermal biofeedback) showed that at 3-year follow-up both groups continued to show lower headache activity, but most in pharmacological group had taken additional medical treatment for their headache compared to the non-pharmacological group. This showed that non-pharmacological reduction in symptoms is more likely to be maintained in the long term without requiring any additional treatment.¹⁷ A randomised controlled trial (RCT) study published in BMJ in 2010 found that managing migraines through combined β blocker and behavioural treatments improved outcomes significantly rather than each alone.¹⁸ A study published in 2011¹⁹ showed adults with migraines/severe headaches used complementary medicine such as deep breathing, yoga more frequently than those without headaches (49.5% years 33.9%, $p < 0.001$). Another study published earlier showed significant improvement in severity, frequency and duration of migraine headaches with repetitive coordinated breathing and movement (known as Kiko in Japanese) as a prophylactic treatment of migraine headaches,²⁰ reduction in medication use by 60% to 62%,²¹ and betterment in headaches.²²

Headache has been an unaddressed cause of morbidity around the world and has remained largely unrecognised in the developing world where 85% of the world's population lives. Most clinical and epidemiological studies have originated in developed countries and there is scarce literature to support treatment guidelines or public health interventions to deal with headache in low and middle income countries. Moreover, there are fewer studies done on the effectiveness of behavioural migraine management in primary care. The current study was

planned to assess the effectiveness of behavioural migraine management in treatment of migraine among adult patients visiting family practice clinics.

Patients and Methods

The single-blinded randomised control trial was conducted from August 2011 to August 2012 at the Aga Khan University Hospital, Karachi, in which adult patients aged 18-65 years were recruited with diagnosis of migraine from five outpatient sites. The study conformed to the Consolidated Standards of Reporting Trials (CONSORT)²³ and approval was obtained from the institutional review committee. Besides, confidentiality of subjects was also maintained and written informed consent was obtained from the study participants.

The subjects fulfilling the International Classification of Disease (ICD-10) criteria were recruited. Those with focal neurologic deficit on examination, patients with language barrier, those who were reluctant regarding telephonic communication, and those who refused to give consent were excluded.

The subjects were divided into two equal groups representing the cases and the controls. The structural behavioural treatment comprised relaxation techniques of deep breathing exercises and progressive muscle relaxation.¹⁷ The trial group was given education material about deep breathing exercises and was advised to perform them daily and to keep a record of it and their symptoms. They received pharmacological treatment, prophylaxis if required, and structured behavioural management. The control group received acute standard pharmacological treatment comprising tablet Paracetamol 1000mg by mouth and tablet Metoclopramide 10mg by mouth,²⁴ while those fulfilling the criteria for prophylaxis were given tablet Inderal 40mg twice daily by mouth.^{24,25} Two training sessions were arranged for doctors participating in the study. During sessions, the doctors were detailed about the study, its objectives, and conduct. They were trained for enrolment of patients in the study, randomisation, administration of intervention and follow-up. Every doctor posted on the clinic was given a number of envelopes containing equal number of intervention and control group's questionnaires.

For randomisation, a statistician prepared predesigned sealed envelopes containing code for intervention or control. To ensure allocation concealment, the envelopes were prepared by a third party not involved in the study. Those enrolled after written informed consent were asked to pick one concealed envelope from the box and hand it over to the doctor concerned. The doctor then assigned

them to either the trial or control group according to the envelope code. Since it was a single-blinded trial, the investigator knew the control and trial groups. The educational material was prepared, reviewed by content expert consultants, and approved by the Joint Commission International (JCI) Patient and Family Education Multidisciplinary Committee. The information was in simple language, relevant to the disease process and management as well as evidence-based.

The same doctor did telephonic follow-up at 2 and 4 weeks after the enrolment of participants for assessing symptoms of frequency, intensity, duration, and effect on QOL.

Two main outcomes were assessed during the follow-up: Primary outcome included change in frequency of migraine attacks, and the frequency was defined as the number of headaches during the intervention period. Secondary outcomes included effect on QOL as well as change in severity of migraine which was assessed through duration of episode and pain scoring on a pain scale during the intervention period. Sample size of 45 patients in each group was required to achieve 90% power to detect a difference of 20%,^{4,5,7,9,25} with 95% confidence interval (CI) and two-sided Z test (pooled variance). The questionnaire was designed after literature search, several brainstorming sessions and focussed group discussion among the residents, medical officers and faculty of the Family Medicine Department. A pilot study was done initially for the questionnaire and educational material validity in which 10% of the sample size was taken which amounted to 5 patients in each group.

Statistical analysis was done using SPSS version 19. Kolmogorov-Smirnov test was used to test the normality assumption for continuous variables like age of the patient, frequency of migraine attacks. Mean and standard errors (SE) of continuous variables were reported because of large sample size ($n > 30$) for each group and applicability of central limit theorem using sampling distribution of mean. Independent samples Z-test was used to compare the difference in mean ages of the participants in the two groups. Percentages with numbers were reported by study groups for categorical data, including gender, level of education and propranol use and the association were observed using Pearson chi-square test.

Repeated Measures analysis of variance (ANOVA) was used to observe the difference in the frequency of migraine attacks and in the severity of pain at baseline, after 2 weeks and 4 weeks of baseline by study groups.

Ordinal logistic regression with clustered robust SEs were

used for QOL and migraine duration at baseline, after 2 weeks and after 4 weeks of baseline by study groups. Where the observations of variables of QOL and migraine duration at different time were treated as cluster to compute standard errors. The odds ratios (OR) with 95% CI were calculated for the treatment effect of the trial group. A P value of 0.05 was considered statistically significant.

Results

Initially, 140 participants were recruited from 5 outpatient clinics. Of them, 110(78.6%) were found eligible after screening. They were randomised into two groups of 55(50%) each. A telephonic follow-up was done at 2 and 4 weeks after which completed data for analysis was available for 90(81.8%) participants (Figure-1). Demographic and medication-related characteristics were separately noted (Table-1). In the trial group, 22(48.9) participants and in the control group 23(51.5) were in the age range of 30-44 years. There was no difference in mean ages of the participants in the two groups ($p=0.388$). Besides, 39(86.7%) in the trial group and 33(73.3%) in the control group were females. In terms of educational status, almost half of the participants, 20(44.4%) in the trial group and 21(46.7%) in the control group were graduate or postgraduate. The use of propranol was almost double in the control group (13; 28.9% vs. 25; 56.8%). No difference was observed in any domain of demographic or medication-related characteristic.

As for the primary outcome, number of migraine attacks among women at baseline, after the 2nd and 4th weeks of baseline showed significant effects of time (Time: $F(2,176)=35.35$; $p < 0.001$; Partial Eta square=0.287)

Table-1: Demographic and Medication-related characteristics.

Variable	Trial Group (n=45) No. (Percentage)	Control Group (n=45) No. (Percentage)	P value
Age (in years)			
18-29	13(28.9)	16(35.6)	
30-44	22(48.9)	23(51.1)	
45-65	10(22.2)	6 (13.3)	
Mean Age (SE)	36.7 (1.5)	34.6 (1.8)	0.388
Gender			0.11
Female	39(86.7)	33(73.3)	
Male	6(13.3)	12(26.7)	
Education Level			0.59
Illiterate	7(15.6)	10(22.2)	
Matric/Intermediate	18(40.0)	14(31.1)	
Graduate/Postgraduate	20(44.4)	21(46.7)	
Use of Propranolol			0.16
Yes	13 (28.9)	25 (56.8)	
No	32 (71.1)	19 (43.2)	

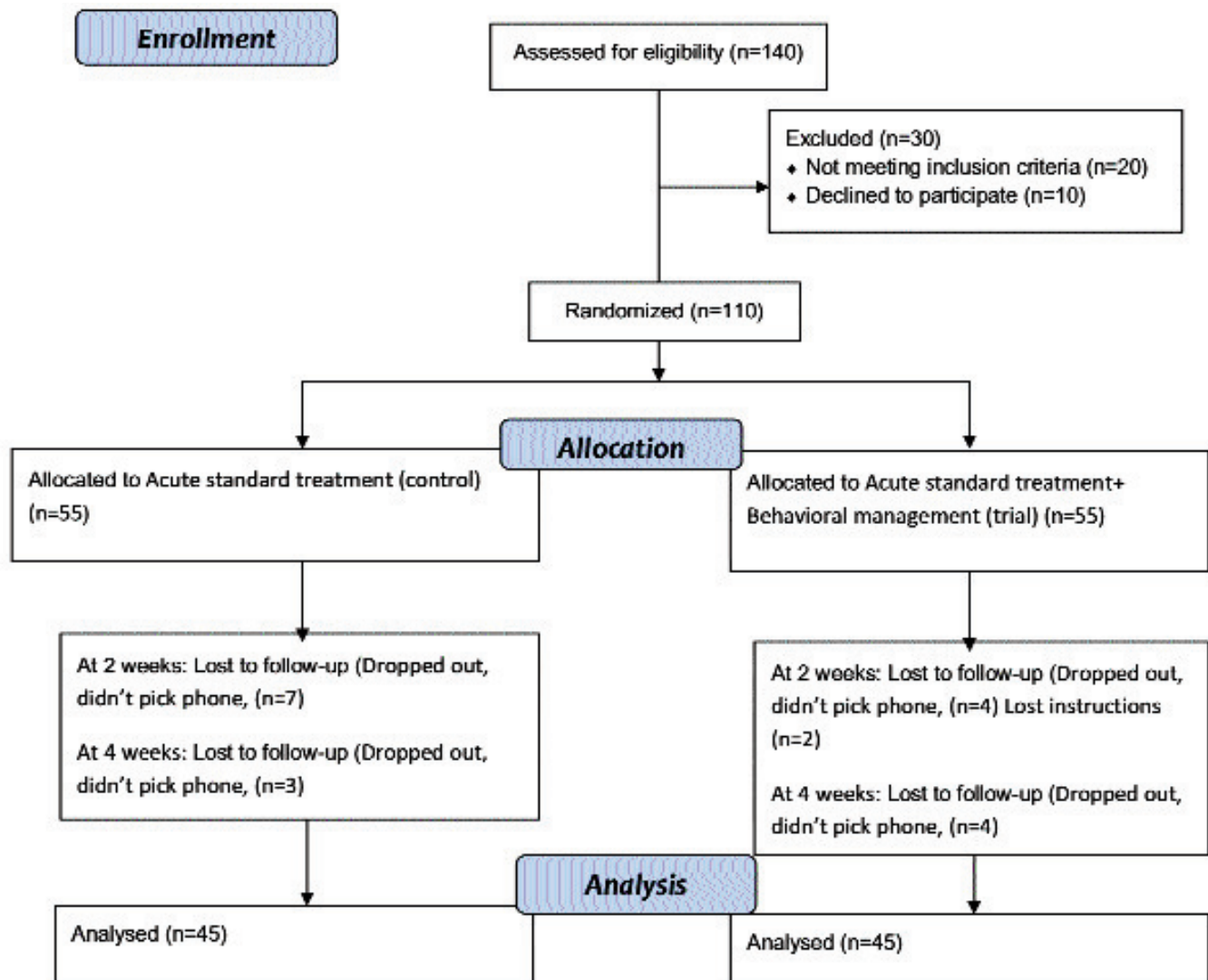


Figure-1: Flow chart of Participants in the trial.

resulting in decline of migraine attacks. Interaction between time and intervention status (Timex Intervention Status: $F(2,176)=7.157$; $p < 0.001$; Partial Eta square=0.075) was also found to be significant in which migraine attacks were more among the treatment group at baseline, but became inverse at 2nd and 4th weeks. No significant effect was found for the intervention status (Intervention Status: $F(1,88)=0.005$, $p < 0.945$; Partial Eta square <0.001) (Figure-2).

Regarding the secondary outcomes, migraine severity was assessed through duration of episode and pain scoring.

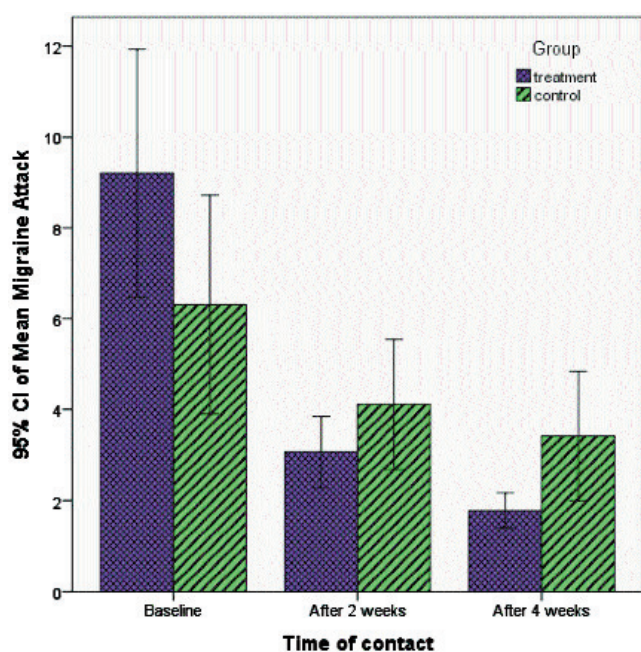
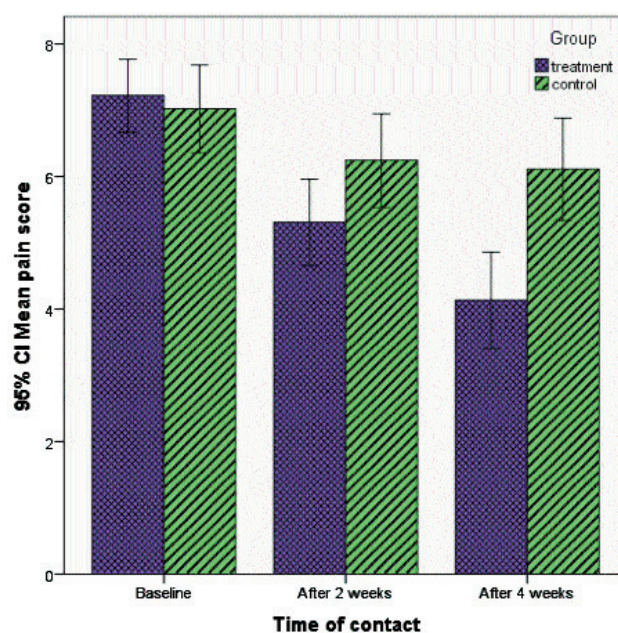
At 2 weeks, 8(17.8%) participants in the trial group and 12

(26.7%) in the control group ($p < 0.762$) reported migraine attack duration of 12-24 hours. At 4 weeks, 3(6.7%) participants in the trial group and 10(22.2%) in the control group ($p < 0.048$) reported their migraine attack duration of 12-24 hours respectively (Table-2).

No significant difference ($p < 0.450$) between treatment type and duration of migraine at different time points was found although the duration of migraine was more among the controls than the trials (Crude Odds Ratio for ordinal outcome=1.25; 95% CI: 0.70, 2.24). Pain scores at baseline, after the 2nd and 4th weeks of baseline showed significant effects of time (Time: $F(2,176)=51.65$, $p < 0.001$; Partial Eta square=0.370), interaction between time and intervention status (Timex Intervention Status:

Table-2: Distribution duration of migraine and quality of life of study participants at different time periods by study groups.

Variable (%)	Trial Group (n=45)			Control Group (n=45)		
	Baseline No. (%)	At 2 weeks No. (%)	At 4 weeks No. (%)	Baseline No. (%)	At 2 weeks No. (%)	At 4 weeks No. (%)
Migraine attack						
Less than 6 hours	1 (2.2)	8 (17.8)	13 (28.9)	4 (8.9)	6 (13.3)	5 (11.1)
6-12 hours	23 (51.1)	27 (60.0)	23 (51.1)	24 (53.3)	25 (55.6)	26 (57.8)
12-24 hours	18 (40.0)	8 (17.8)	3 (6.7)	13 (28.9)	12 (26.7)	10 (22.2)
More than 24 hours	3 (6.7)	2 (4.4)	6 (13.3)	4 (8.9)	2 (4.4)	4 (8.9)
Quality of life						
Extremely	19 (42.2)	1 (2.2)	1 (2.2)	21 (46.7)	16 (35.6)	17 (37.8)
Moderately	25 (55.6)	28 (62.2)	10 (22.2)	20 (44.4)	22 (48.9)	22 (48.9)
Very little	1 (2.2)	14 (31.2)	23 (51.5)	4 (8.9)	6 (13.3)	3 (6.7)
Not at all	0 (0.0)	2 (4.4)	11 (24.1)	0 (0.0)	1 (2.2)	3 (6.7)

**Figure-2:** Mean number of Migraine attacks reported by patients (95% Confidence Interval) by Time of contact and treatment group.**Figure-3:** Mean pain score reported by patients (95% Confidence Interval) by Time of contact and treatment group.

$F(2,176)=17.38$, $p<0.001$; Partial Eta square=0.143) and for intervention status (Intervention Status: $F(1,88)=4.65$, $p=0.034$; Partial Eta square=0.050) (Figure-3).

At 2 weeks, pain score was 5.31 ± 2.15 in the trial group and 6.24 ± 2.34 in the control group ($p=0.052$). At 4 weeks, it was 4.13 ± 2.42 in the trial group and 6.11 ± 2.57 in the control group ($p<0.001$).

At 2 weeks, QOL was reported to be affected extremely by 1 (2.2%) participant in the trial group and by 16 (35.6%) in the control group ($p<0.001$). At 4 weeks, QOL was reported to be affected extremely by 1 (2.2%) participant in the trial group and by 17 (37.8%) in the control group

($p<0.001$) (Table-2).

A significantly better QOL ($p<0.001$) was observed among the trial group compared to control group (Crude OR =3.80; 95% CI: 2.09, 6.91). None of the participants in the study reported any side effects or harms by the treatment given.

Discussion

The randomised controlled trial evaluated the effectiveness of behavioural management on migraine headache. Behavioural management has a beneficial effect on various migraine parameters such as frequency, severity of migraine attack and QOL improvement.

Migraine is affected by complex relationships between biology, environment, behaviour, cognition, and emotions; therefore, behavioural medicine has its role in the treatment.^{12,13} Once behavioural treatments and techniques are learned, patients can utilise their skills in recognising and mediating the effects of stress at any time and in any context.^{12,13} The frequency of the migraine attacks was significantly decreased after four weeks of acute treatment and behavioural migraine management. This result is consistent with a similar study in which the addition of combined beta blocker and behavioural migraine management improved on the outcomes obtained with the optimised acute treatment.^{16,20} Although the reduction in pain severity after two weeks of acute treatment and behavioural management was not statistically significant, but the results were highly significant after four weeks ($p < 0.001$).¹⁶ This can be explained by the fact that behavioural treatment may have taken a longer time to set in than medications, but research suggests that the effect may be more durable because they also address other problems.¹⁰ The addition of behavioural management improved the QOL not only at two weeks but after four weeks also ($p < 0.001$). Although we had not used the measurement scales,⁶ which had been used for measuring QOL, the participants reported their perceptions. Further studies in the primary care settings can be done by employing these measurement scales. This was one of the few controlled trials to examine the effects of behavioural migraine management with optimised acute treatment in a developing country. This may be a cost-effective way of treating migraine by avoiding the side-effects.²⁰ Since the patients who sought advice were in their most productive age, this may be a hopeful, cost-effective and safer approach of improving outcomes in the management of migraine.^{5,20} However, since both the groups received the acute and prophylactic treatment, the advantages obtained by behavioural management alone can be lessened. Nevertheless, this trial was not designed to evaluate the effectiveness of the acute treatment, thus did not include a comparison group that did not receive either acute treatment or preventive treatment. This would have been un-ethical because of the psychosocial and biological effects of frequent disabling migraine.¹⁶

In terms of study's limitations, the majority of the participants were females. One of the reasons could be that the doctors who had collected data were females and in our culture female patients prefer to have consultation with female doctors and, secondly, it is evident that migraine is more prevalent in females. We evaluated only two methods of behavioural management of migraine,

that is deep breathing exercises and progressive muscle relaxation. In addition, our findings are limited to preventive treatment with beta-blocker drugs only. However, little evidence indicates that other preventive drugs, including antidepressants and anticonvulsants, are more effective than β blockers for episodic migraine¹⁶ and also adequately powered comparisons of different preventive drugs are unavailable. Similarly, adequately powered comparisons of different behavioural interventions also are unavailable.¹⁷ Thus, these findings may be generalisable to other preventive drugs and to other behavioural interventions. However, appropriately designed clinical trials are needed to overcome this limitation. It was a single-blinded trial since the investigators were involved in the data collection and it was conducted at one hospital only. Moreover, there is a possibility of cross-contamination when the individuals were randomised to the intervention and control groups and were exposed to the opposite condition (intervention/control) through contact with each other.

Conclusion

Combination of behavioural migraine management and acute treatment in this trial improved the clinical outcome. Behavioural management may be a hopeful method for improving treatment outcomes and for reducing the progression of migraine. It is recommended that family physicians should incorporate behavioural management in the treatment of migraine patients in order to provide safe, cost-effective and convenient care.

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