

Quality of Life of Migraine Patients Treated With Combined Propranolol and Topiramate

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Background: Migraine is a chronic neurological disorder, which affects the quality of life (QOL). The burden of this disease could be improved by adequate prophylactic treatment.

Objectives: We aimed to assess the quality of life in patients with migraine treated with both propranolol and topiramate in Shiraz, Iran.

Patients and Methods: In this interventional study, we enrolled 100 newly diagnosed migraine patients who were referred to multidisciplinary clinic of Motahari in Shiraz. Reliable and valid Persian SF-36 questionnaire were used for the evaluation of baseline health-related QOL (HRQOL) and after treatment with 25 mg topiramate (twice daily) and 20 mg propranolol (three times daily) as prophylactic treatment. We used SPSS version 13 for data entry and analysis.

Results: Scale differences were statistically significant in all scales before and after the intervention, except in vitality scale. After treatment, the highest score belonged to physical problem and the lowest one was emotional problem. Men had significantly higher scores in body pain compared to women ($P = 0.039$).

Conclusions: Combined migraine prophylaxis with propranolol and topiramate improved HRQOL in migraine sufferers in our study. Adequate prophylaxis improved especially physical problem scale, which manifests with better performing activity and work. More study on the effect of monotherapy along with combined therapy with different doses on HRQOL may be helpful to further evaluate this effect.

Keywords: Migraine; Topiramate; Propranolol

1. Background

Migraine is a chronic neurological disorder which is characterized by recurrent attacks and return to baseline condition between attacks, which affects 11% of adults worldwide (1, 2). Migraine doubles the risk of ischemic stroke in patients with aura (3). Migraine patients (MPs) bear fear of disruption of their working ability, failure to meet family or social responsibilities, and other psychosocial stresses in a way that affects their quality of life (QOL) and work productivity more than many other chronic diseases (4, 5). Treatments could reduce frequency and pain severity of migraine, which consequently can decrease the medical cost and burden of disease (6). Appropriate medical management for MP varies as acute, prophylactic, or both, and best approach is chosen according to the clinical setting (7). Many of MPs only need treatments for acute attacks but others need prophylactic treatment; indications for prophylactic treatment are present elsewhere (7, 8). Appropriate prophylaxis is important for reducing disability and preventing progression of the disease into a chronic progressive illness (9). The goal of treatment in migraine is improving QOL

(2, 6). There are different ways for assessing QOL, which is aimed by this study. By assessing QOL, we could understand the impact of treatment or effects of the disease on patients' QOL (10).

In a population based study in London, a short form 36-Item health survey (SF-36) for assessing HRQOL of migraine sufferer was used, significantly had lower scores in most scales of the SF-36 compared with the control group while greater reduction in HRQOL was seen in patients with more disability was identified (11). In another population based study in France, more than half of the migraine sufferer stated adverse impact of migraine on their daily living (12). There are plenty of studies on the effect of therapeutic or prophylactic management of the migraine on HRQOL. In a study in the USA, the effect of treatment with topiramate as the prophylactic treatment of migraine on QOL showed significant improvement of the QOL in the treatment group compared to the control group (13). In another study, the effect of the treatment with propranolol versus behavioral management was assessed; combination of propranolol and behavioral man-

agement had positive effect on the QOL (14). Although, single drug treatment has been extensively studied, a few studies have evaluated the effect of combined prevention treatment with two or more drugs. As in a randomized control trial (RCT), propranolol was added to topiramate in patients with inadequate controlled chronic migraine with topiramate alone, showed no adequate evidence for its benefits (15), while another RCT showed the effectiveness of the combined nortriptyline and propranolol in migraine prophylaxis (16). Theoretically, combined drug therapy could have more advantages, because each drug could pathophysiologically targets different aspects of the disease (17).

2. Objectives

To the best of our knowledge, there was no similar study on this topic in Shiraz. Regarding high burden of migraine and importance of effective prophylaxis on QOL of patients, we decided to assess the quality of life of MPs treated with both propranolol and topiramate in our region.

3. Patients and Methods

This interventional study has been performed in Shiraz, the center of Fars Province in south Iran. We enrolled 100 newly diagnosed migraine patients who were referred to Motahari Clinic (a multidisciplinary popular clinic in Shiraz) in year 2011. The study sample was selected from patients older than 15 years, receiving care due to their headache in three days of week. Then, migraine was diagnosed by a neurologist who was the faculty member of Shiraz University of Medical Sciences and prophylaxis was prescribed by this neurologist according to the indications. If there were no contraindication, a prophylactic treatment would be started containing 25 mg topiramate (twice daily) and 20 mg propranolol (three times daily). We excluded the patients with concurrent disease or taking medication regularly for another disease. When the patients signed the informed consent, they were given a questionnaire consists of two parts; first part had questions about demographic factors and the second part was a reliable and valid Persian SF-36 (18). This questionnaire was filled at baseline by face to face interview with migraine patients. Each interview lasted 10-15 minutes.

Patients were also informed that the continuity of the treatment would not be affected if they did not have consent to participate in the study. After at least two months of appropriate consumption of prophylactic treatment (which were asked through follow-up phone call), SF36 questionnaire was again filled through phone call. SF36 questionnaire yields 36 items, which collectively build up an 8-scale profile of scores. These 8 scales included: 10 items for physical functioning (PF), 2 items for social functioning (SF), 4 items for role limitation (physical problems [RP]), 3 items for another role limitation (emotional problems [RE]), 5 items for mental health (MH),

4 items for vitality (V), 2 items for body pain (BP), and 6 for general health perception (GH). Each one of 36 items was scored then summed up, which ranges from the scale of 0 (worst health status) to 100 (best health status) and then standardized using SF-36 protocol. Data were entered in SPSS program version 13 and 1-way analysis of variance (ANOVA) and independent sample t test were used for data analysis. P value < 0.05 was considered as significant.

4. Results

Tables 1 and 2 present characteristics of the disease and participants are. All patients had higher scores in 8 scales of HRQOL after treatment. These scale differences (before and after treatment) were statistically significant in all scales, except in vitality scale. After treatment, the highest score belonged to RP and the lowest was RE. Mean scores and P values for differences of 8 scales of HRQOL, before and after treatment has been presented in Table 3. Improvement of mean HRQOL scores had no significant correlation with age. Comparison of the changes in scores of HRQOL scales in migraine patients regarding different sexes showed that men had significantly higher scores in BP scale compared to women ($P = 0.0390$), but other sales were not significantly different. Results showed that improvement in HRQOL did not have significant correlation with marital status of the patients; however almost all improved mean scores after treatment were higher in married patients. Improvement in mean scores of HRQOL was neither significantly correlated with the length of the disease nor with the duration of the treatment. Correlation between the number of attacks and change in HRQOL was significant in physical problems ($P < 0.001$), body pain ($P = 0.001$), general health perception ($P = 0.001$), social functioning ($P = 0.015$) scales, i.e. increase in the number of attacks is correlated with the rise of mean scores.

Table 1. Participants' Characteristics

Variable	Value	Total
Gender		100
Male	26	
Female	74	
Marital status		100
Single	25	
Married	75	
Education		100
< High school	35	
High school	23	
University	42	

Table 2. Disease Characteristics of Participants^a

Variable	Value
Age, y	34.13 ± 10.79
Min	19
Max	64
Frequency of attacks, mo	6.23 ± 6.68
Min	1
Max	30
Duration of disease, y	4.98 ± 5.01
Min	0.1
Max	26

^a Data are presented as Mean ± SD.

Table 3. Comparison of Scales of HRQOL in Migraine Patients Before and After Prophylaxis^a

Scales	Before Treatment	After Treatment	P Value
Physical functioning	76.15 ± 25.45	76.40 ± 25.32	0.025
Physical problems	34.00 ± 41.21	89.50 ± 26.86	< 0.001
Body pain	39.30 ± 17.42	76.50 ± 11.31	< 0.001
General health perception	53.40 ± 22.04	55.64 ± 20.76	< 0.001
Vitality	52.30 ± 19.81	52.90 ± 19.20	0.116
Social functioning	75.50 ± 21.90	64.62 ± 20.10	< 0.001
Emotional problems	36.66 ± 43.03	45.00 ± 45.53	0.002
Mental health	59.20 ± 18.86	59.64 ± 18.18	0.040

^a Data are presented as Mean ± SD.

5. Discussion

HRQOL improved after combined prophylactic treatment with topiramate and propranolol in all scales in migraine patients and this was statistically significant, except in vitality scale. It is probably due to the reduction in the frequency or severity of the attacks, so that MPs need shorter time for staying in bed or rest. Consequently, this could affect the overall physical condition and social relationships of the patients. Study on the impact of combined therapy of migraine on HRQOL is scarce. One study evaluated the effect of combined propranolol (up to 240 mg/day) and topiramate (up to 100 mg/day) prophylactic treatment on migraine severity. It neither showed added effect of this combination in decreasing the frequency of headache nor its severity (15). Another study for evaluation of presence or intensity of headache showed that

propranolol was effective both alone and in combination with nortriptyline (16).

Another study in the United States, assessing the effect of topiramate on HRQOL in chronic migraine, showed reductions in the limitations related to migraine on daily activities and emotional distress (19). A randomized, double-blind, placebo-controlled multicenter trial on the effect of administering topiramate on HRQOL also showed that topiramate significantly improved mean SF36-RP domain scores vs. placebo after treatment, and patients had improved SF36-VT domain scores, although not significantly compared to placebo which was similar to our study (20). Vitality did not change significantly after treatment of MP, maybe due to fatigue as complications of topiramate and propranolol (7).

Our study showed that physical problem was the least scored HRQOL scale before the treatment and had the highest increase after prophylactic treatment. This scale indicates whether patients had problem for performing their activity and work; so this is an appropriate outcome which shows decrease in physical problems after prophylactic treatment. In this study, men had significantly more changes in BP scores compared to women and other scales were not significantly different. This result is probably due to the influence of sex hormones such as estrogen in women or because women are more influenced by psychosocial or familial factors (21, 22).

The least score after treatment belonged to RE, probably due to the complication of the treatment or the relation of migraine with other psychosocial difficulties such as anxiety, depression, anger, or stress (23). Probably, considering psychosocial variables addressing the routine healthcare practices for migraine patients is necessary. It has been shown that migraine treatment could diminish the psychosocial problems of migraine patients by decreasing the frequency of attacks (23). Because subjective expectations has been mentioned for assessing experienced quality of life, precise training of the patients to change lifestyle and enhanced compliance with prescribed treatment and self-care are critical in chronic disease management like migraine for a better experienced HRQOL. To the best of our knowledge, this study is the first study in our region on the effect of combined migraine prophylaxis on HRQOL. However further study on the effect of this combination along with monotherapy with different doses on HRQOL is also suggested. It is to be noted that SF-36 questionnaire is not specific to migraine and may reflect problems related to other conditions rather than migraine.

Combined migraine prophylaxis with propranolol and topiramate improved HRQOL in migraine sufferer of our study. Adequate prophylaxis has improved physical problem scale more, which showed better performing activity and work in MPs. More studies on the effect of monotherapy along with combined therapy with different doses on HRQOL may be helpful for further evaluation of this effect.

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Authors' Contributions

All authors contributed equally in preparing the article.

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