Iranian Journal of Pharmaceutical Research (2004) 4: 215-223
Received: April 2004
Accepted: August 2004

Original Article

The Effect of Gabapentin on Withdrawal Syndrome, Psychiatric Disorders and Electroencephalogram of Opium Addicts during the Detoxification Period

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Abstract

Substance abuse is an important health, psychological and social problem in the world. Gabapentin is a new antiepileptic drug. It is used in neurological and psychiatric disorders. Moreover the effects of gabapentin on increasing the analgesic effect of morphine and its inhibitory effects on dopamine release due to morphine in animal models have been proved. In the present study, the effect of gabapentin on withdrawal signs and symptoms in opium-addicted participants and on psychiatric disorders and electroencephalogram of these patients during the detoxification period has been investigated. Two groups of patients were selected randomly. The first group (n=36) received the current drugs based on their withdrawal symptoms and the second group (n=35) received an additional 900 mg gabapentin daily. All the patients were evaluated by electroencephalography and Symptom Check List-90-Revised on the first and last days of hospitalization and their demographic characteristics were gathered by using a general questionnaire. During the hospitalization period (10 days) all the patients were visited daily for withdrawal signs and symptoms. The analysis of data showed the excellent effect of gabapentin on all psychiatric symptoms and in decreasing signs and symptoms significantly. A gradual decrease of withdrawal signs and symptoms in the second group shows the efficacy of gabapentin. There was no significant difference between the two groups, regarding to the electroencephalogram indices. The results show that gabapentin improves the quality of therapeutic management in opium-addicts during the detoxification period.

Keywords: Gabapentin; Opium; Detoxification period; Electroencephalogram; Symptom Check List-90-Revised.

Introduction

Addiction apart from being a hygienic and social problem is like a recurrent chronic brain disease, since it has certain effects on brain function. Substance abuse leads to special cellular change, as well as neurotransmitter and chemical activities in neurons and receptors (1).

Two large studies have shown a higher prevalence of psychiatric diseases among addicts, compared with the common population (2, 3). The most common disorder in treatment seeking opiate dependent patients is major depression (lifetime 53.9%, current 23.8%)(4). However, in producing addiction, in addition to psychopathologic factors, biologic, social and environmental factors also have important roles (5).

In opioids abuse and dependency some neurons, receptors, chemical transmitters and cerebral organs play various roles. Opioid receptors in all parts of brain, digestive system and other parts of autonomic system have been discovered and it is not surprising if opioids

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Table1. Mean and frequency of demographic features in groups G and C.

Variable	Group		
	G (n=35)	C (n=36)	P value
Marital status			
Single	7 (20)	18 (50)	
Married	27 (77.1)	18 (50)	0.013
Missing	1 (2.9)	0	
Job status			
Employed	23 (67.6)	33 (91.7)	
Unemployed	11 (32.4)	3 (8.3)	0.012
Missing	1	0	
Job			
Self-employed	19 (82.6)	29 (87.9)	
employee	4 (17.4)	2 (6.1)	0.22
Non-official employee	0	2 (6.1)	
Type of opium consumption			
Oral	4 (12.1)	12 (33.3)	
Smoking	21 (63.6)	16 (44.4)	
Injection	1 (3)	1 (2.8)	0.23
Oral & smoking	7 (21.2)	6 (16.7)	
Oral & injecting	0	1 (2.8)	
Mean years of consumption	8.86 ± 5.33	8.9 ± 6.58	0.085
History of drug quit	27 (81.8)	24 (66.7)	0.09
Number of drug quit	2.93 ± 4.41	2 ± 2.2	0.24
Desire for using new drug for drug quitting	35 (100)	33 (91.7)	0.085
History of epilepsy	0	2 (5.6)	0.27
History of drug allergy	2 (6.1)	4 (11.1)	0.45
Consumed drugs			
None	24 (70.6)	19 (52.8)	
TCA	4 (11.8)	10 (27.8)	
NSAID	0	2 (5.6)	
Benzodiazepines + TCA	4 (11.8)	4 (11.1)	*0.52*
Benzodiazepines + NSAID	1 (2.9)	0	
TCA + NSAID	0	1 (2.8)	
All three drugs	1 (2.9)	0	

All patients (or researchers) recorded their demographic features by using a g eneral questionnaire, on admission.
NS: Not Significant

cause alteration in the functions of most body systems (6). These substances have also significant effects on noradrenergic and dopaminergic neurotransmitter systems (7).

Some studies have shown that opium compounds exert their reinforcement and rewarding effects via activating dopaminergic neurons in the tegmental area, which extends toward cortex and limbic system (7). Naturally GABA has an inhibitory effect on these neurons and morphine increases dopamine via its inhibitory effect on GABA (5).

Long-term consumption of opioid compounds alters the number and sensitivity of opioid receptors which are the mediators of some drug dependency and quit effects (7). Dependency occurs in long-term substance consumption, which is accompanied by an increase in the sensitivity of dopaminergic, cholinergic and serotoninergic neurons. It is possible that the main mediator of drug quit is the effect of opioid substances on noradrenergic neurons (7).

Drug quit after long-term consumption of opioid compounds leads to symptoms called withdrawal syndrome. This is the result of irritability in different parts of central nervous system and similar to seizure in this aspect. Even the electroencephalogram of drug quitters is affected and in 50% of drug quitters significant changes in EEG have been observed (8). In another study, quantitative electroencephalographic (QEEG) of 90 patients with substance abuse who had not used any substance for an average of 3 months was investigated and a decrease in the intensity of Alpha and Beta waves in comparison to normal state was observed (9).

Various therapeutic methods have been suggested for drug quit, but none of them has led to complete satisfaction of patients with regard to the control of withdrawal symptoms during the detoxification period. Generally the suggested protocols for drug quit are divided

Table 2. Mean total score of withdrawal signs during ten days after drug quit in the groups G and C.

Variable	group G (n=35)	group C (n=36)	P-value
Yawning	9.03 ± 4.79	13.69 ± 5.45	0.0001
Lacrimation	3.94 ± 4.2	8.28 ± 6.37	0.001
Rhinorrhea	5.17 ± 4.94	6.47 ± 5.58	0.33
Sweating	4.66 ± 4.67	7.72 ± 5.75	0.016
Tremor	4.91 ± 5.38	6.53 ± 5.04	0.088
Piloerection	2.69 ± 3.62	4.78 ± 5.32	0.077
Restlessness	8.4 ± 5.82	10.56 ± 5.73	0.12
Pupil size	35.83 ± 9.27	37.87 ± 6.67	0.314
Vomiting	0.74 ± 1.63	0.83 ± 2.25	0.771
Diarrhea	2.6 ± 3.58	2.92 ± 3.54	0.65
Insomnia	6.86 ± 5.98	8.58 ± 5.43	0.208
Drug seeking	2.37 ± 3.57	1.92 ± 2.25	0.941
Anorexia	5.03 ± 5.48	5.89 ± 5.73	0.485

All patients were examined daily (in an exact time) for the above-mentioned signs and scored based on the absence (0), probable presence (1) or clear presence of signs (2). Each point is the mean ±SEM over ten days.
There were significant differences between the two groups in yawning, rhinorrhea ($p<0.01$), and sweating ($p<0.05$).

into two groups: Conservative treatment with morphine agonists (e.g. methadone) and treatment by using drugs without opioid properties (e.g. clonidine)

Gabapentin (GBP) is a new anticonvulsant drug used as an adjunctive therapy in partial seizures (10). Based on experimental studies, GBP prevents maximal electroshock convulsions and seizures due to electrical kindling, pentylenetetrazol, thiosemicarbazide and isoniazid (11). GBP has other uses also. In a study in mice, gabapentin was found to control both anxious and convulsive symptoms of alcohol withdrawal (12). Even alcohol-quit patients have benefited from GBP and clomethiazole dosage has been decreased in them (13). It is probable that the GBP effect is related to an increase of GABA and decrease of glutamate system in the central nervous system (14). Gabapentin as an analgesic has a broad spectrum of efficacy in neuropathic pains (15). Based on some studies, GBP increases the analgesic effect of morphine, such that smaller doses of morphine are needed. This effect is related to μ receptors (16).

Moreover GBP has been recognized as a mood stabilizer (17). The other study showed that gabapentin might be a useful drug for the add-on treatment of bipolar patients with incomplete response to other mood stabilizers (18). However, studies on its efficacy in the treatment of anxiety disorders or substance abuse are limited (17). In a study, GBP has been introduced as an important adjuvant to the management of opioid dependence in both acute detoxification as well as stabilization phase (19). In another study, GBP has been found as the first preemptive antihyperalgesic in the treatment of hyperalgesia for opioid withdrawal syndrome (20).

In the present study, the efficacy of GBP in the treatment of opioid dependent patients has been investigated. For this purpose, the effect of GBP on opioid withdrawal signs and symptoms and the psychiatric disorders and EEG of patients during the detoxification period were studied. Owing to ethical considerations, the action of gabapentin was tested in add-on manner in addition to other usual medications used in opioid withdrawal syndrome (clonidine, benzodiazepines, NSAID, and diphenoxylate in case of need). There is no pharmacological interference between these drugs and GBP. All the patients gave an informed consent to participate in this study.

Experimental

Patients

In this prospective clinical trial study, 71 opium-dependent participants (opium and other forms) hospitalized in Kerman Psychiatric Hospital were selected randomly and divided into two groups of G (gabapentin and usual drug quit medication, N=35) and C (only usual drug quit medication, N=36).

Data gathering

In admission, demographic features of participants were recorded by using a general check list. Females were excluded because of

Table 3. Mean total score of withdrawal symptoms during ten days after drug quit in the groups G and C.

Variable	G group (n=35)	C group (n=36)	P
Muscle crump	3.14 ± 4.53	3.08 ± 4.59	0.928
Palpitation	3.63 ± 5.17	4 ± 5.24	0.532
Sneezing	7.57 ± 5.24	13.87 ± 5.18	0.0001
Pins & needle sensation	3.28 ± 4.42	7.11 ± 6.3	0.009
Hot & cold flashes	5.6 ± 5.97	12.28 ± 5.27	0.0001
Goose flesh	1.54 ± 3.5	2.89 ± 3.64	0.019
Feeling of sickness	5.89 ± 6.11	6.89 ± 5.98	0.424
Stomachache	3.97 ± 15.16	7.72 ± 7.11	0.047
Skeletal & muscular pains	6.97 ± 6.55	11.11 ± 5.38	0.005
Muscle twitching	4.28 ± 5.64	7.8 ± 4.95	0.001
Irritability	6 ± 5.93	8.44 ± 5.76	0.083
Craving	7.74 ± 5.01	6.39 ± 5.56	0.285

The history of all patients were taken daily (in an exact time) for the above-mentioned symptoms and scored based on the absence (0), probable presence (1) or clear presence (2) of symptoms.
Eeach point is the mean ± SEM over ten days.
There were significant difference s between the two groups in terms of sneezing, pins & needle sensation, hot & cold flashes, skeletal & muscular pains, muscle twitching ($p<0.01$), gooseflesh and stomachache ($p<0.05$).

the low prevalence of addiction among them and also in order to omit the probable intervening effect of some drugs such as oral contraceptives consumed by some women.

Two electroencephalograms, one at the onset and one at the end of hospitalization period were requested for all participants.

Group C received the usual medication for drug quit [clonidine as the main drug (0.4-0.8 mg/d); NSAIDs as analgesic (Ibuprofen, 1200mg/d); benzodiazepines (Lorazepam, 2-6 mg/d); tricyclic antidepressants (Amitriptyline, 25-75 mg/d); Promethazine 25-50 mg/d; Diphenoxylate PRN].

Group G in addition to the usual medications, received 900 mg gabapentin daily, divided into three doses, for 7-10 days.

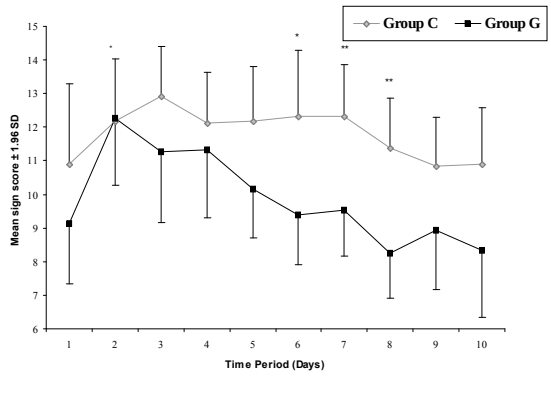

Figure 1. Mean total score of withdrawal signs during ten days after drug quit in the groups G and C.
* $P<0.05$ on the second and sixth days, the total score of withdrawal signs shows a significant difference between groups G and C.
** $P<0.01$ on the seventh and eighth days, the total score of withdrawal signs shows a significant difference between groups G and C.

All participants were evaluated by SCL-90-R at the onset and end of the hospitalization period.

Electroencephalography

Electroencephalography was performed by electroencephalogram (HELLIGE, Neuroscript, 8 channels) in awake state.

General check List

This was filled out by participants themselves or the researcher and contained questions related to job status ,type of job, monthly income, marital status, educational level, number of sisters and brothers, birth order in the family, type of the consumed narcotic, type of consumption, the amount of daily use (g), the duration of consumption, history of drug quit, tendency for using the new drug for quitting, history of epilepsy, history of drug allergy and the consumed drugs.

Check List for withdrawal signs and symptoms

This check List contains 13 signs (yawning, lacrimation, rhinorrhea, sweating, tremor, piloerection, restlessness, pupil size, anorexia, vomiting, diarrhea, insomnia, and drug seeking) and 12 symptoms (muscle cramp, palpitation, sneezing, pins and needle sensation, hot and cold flashes, gooseflesh, feeling of sickness, stomachache, muscular and skeletal pains, muscle twitching, feeling of irritability, and craving) (21).

All participants were visited and given daily

Table 4. Mean of SCl-90 scores in the first & tenth days after drug q uit in the G and C groups

SCL-90 index	Group G (n =35)			Group C (n = 36)		
	First day	Tenth day	P-value	First day	Tenth day	P-value
Aggressiveness	1.32±0.98	0.75±0.89	0.0001	1.09±0.75	1.11±1.03	0.715
Anxiety	1.58±1.18	0.86±0.88	0.0001	1.3±0.8	1.05±0.75	0.075
Depression	1.89±1.04	0.96±0.10	0.0001	1.73±0.95	1.13±0.75	0.0001
Sensitivity to interpersonal relations	1.7±1.10	1.37±3.42	0.0001	1.52±0.8	1.10±0.78	0.001
Obsession & compulsion	1.54±0.95	0.92±0.86	0.0001	1.26±0.78	1.01±0.82	0.107
Somatic compulain ts	1.32±0.96	0.78±0.75	0.0001	1.08±0.67	1.06±0.67	0.872
Phobia	0.97±0.95	0.49±0.66	0.0001	0.76±0.66	0.73±0.75	0.169
Paranoia	1.74±1.03	1.06±0.85	0.0001	1.57±0.72	1.23±0.81	0.013
Psychosis	1.14±0.82	0.74±0.73	0.0001	1.11±0.66	0.89±0.66	0.083
Additional questions	1.28±1.11	0.99±0.85	0.131	1.04±0.72	1.04±0.8.	0.992
GSI	1.44±0.89	0.86±0.73	0.0001	1.28±0.64	1.00±0.67	0.024
PSDI	2.15±0.63	1.76±0.63	0.003	2.07±0.51	1.62±0.75	0.003
PST	52.2±24.75	32.66±23.99	0.0001	52.14±23.03	49.40±25.03	0.516

The researchers evaluated all patients for the psychiatric disorders at the time of admission and discharge, based on the Scl -90-R indices.

There were significant differences between the first day and tenth day in all indices in G group ($p<0.01$) and in group C, for de pression, sensitivity in interpersonal relations ($p<0.01$), and paranoia ($p<0.05$).

NS: Not significant, GSI: General Symptomatic Index, PSDI: Positive Symptom of Distress Index, PST: Positive Symptom Total, SCL-90: Symptom Check List–90 revised

scores for the above-mentioned signs and symptoms.

Symptom Check List-90-Revised (SCL-90-R)

SCL-90-R was used for evaluating the psychiatric disorders at the time of admission and discharge.

With this test, nine aspects (somatic complaints, obsession and compulsion, sensitivity to interpersonal relations, depression, anxiety, aggressiveness, phobia, paranoia, and psychosis) are measured and analyzed based on the following indices: 1-General symptomatic index (GSI), 2-Positive symptom of distress index (PSDI), 3-Positive symptom total (PST).

SCL-90-R as a successful diagnostic method is widely used through the world in patients with alcohol/narcotic dependency, sexual disability, cancer, heart failure, severe organic diseases and those who need consultation (22-24).

Statistical analysis

After data collection, they were analyzed by SPSS and Stata v.7 computer softwares (power 80%, Confidence Interval 95%). Nominal and ordinal variables were compared in two groups (G and C) by Chi-square test or the Fisher Exact test.

Mean total score of withdrawal signs and symptoms were compared by the Mann-Whitney U test. Wilcoxon nonparametric test or paired sample test was used for comparing the score of first and tenth days. One sample Kulmogorov-Smirnov was used to test normal distribution. EEG type in first and tenth days was evaluated in two groups by the Mc-Nemar test. ANOVA, Repeated measures and Tukey Post-Hoc were used for comparing variation of scores of withdrawal signs and symptoms during detoxification period.

Results and Discussion

Demographic features

Mean age of group G (N=35) was 33.49±7.33 years and that of group C was 30.97±12 years and there was no significant difference between the two groups (p=0.94).

Most participants in the two groups had more than five brothers and sisters (p=0.86) and they were not the first child in their family (p=0.77). There was no significant difference between the two groups regarding their monthly salary (p=0.80).

The consumed narcotic drugs in both groups were heroine and opium, and the type of consumption was mostly smoking. The amount of consumption was 2.36±1.85 g in group G and 5.02±1.78 g in group C with no significant difference (p=0.08). Most participants in both groups had been addicted for more than one year.

Table 1 shows some of the demographic features of participants.

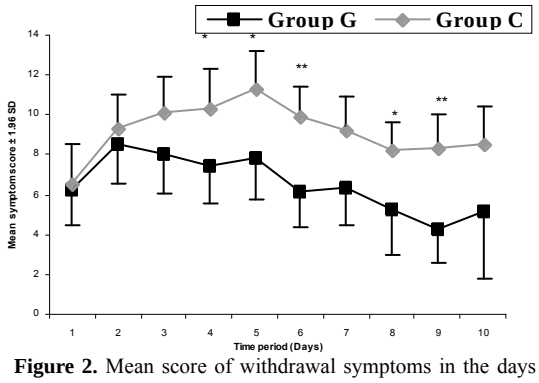

Figure 2. Mean score of withdrawal symptoms in the days after drug quit in the groups G and C.
* P<0.05 Significant difference between groups G and C regarding the total score of withdrawal symptoms on the fourth, fifth, seventh and eighth days.
** P<0.01 Significant difference between groups G and C regarding the total score of withdrawal symptoms on the sixth and ninth days.

There were only two significant differences between the two groups which were in terms of the marital and job status, this can not be explained from the available data. But with all the other items, there was no significant difference.

Withdrawal signs and symptoms during the 10 days of treatment

I) Withdrawal signs

In group G scores of yawning (9.03±4.7 times), lacrimation (3.94±4.2) ($p<0.01$) and sweating (4.66±4.67) ($p<0.05$) were significantly lower than those of group C (Table 2).

II) Withdrawal symptoms

In group G, scores of sneezing (7.57±5.24), pins and needle sensation (3.28±4.42), hot and cold flashes (5.6±5.97), muscular and skeletal pains (6.97±6.55), muscle twitching (4.28±5.64) ($p<0.01$), gooseflesh (1.54±3.5), stomachache (3.97±5.16) ($p<0.05$), were significantly lower than those of group C (Table 3).

In studying the results of withdrawal signs and symptoms based on the check list (21), some signs such as rhinorrhea, yawning, sweating and also some symptoms such as sneezing, pins and needle sensation, hot and cold flashes, gooseflesh, stomachache, muscular and skeletal pains, and muscle twitching showed a significant decrease in the gabapentin-treated group. With regards to diarrhea, vomiting, muscle cramp and palpitation, with a power of <0.7 and an increase in sample, a significant difference between the two groups would be expected. Mean score of the withdrawal signs and symptoms showed a decrease in both groups during the process of treatment, but this decrease started earlier and continued more rapidly in group G compared to group C. This means that in group G, mean score of all days (except the tenth day) were lower than those in group C. In group G, mean score of the last three days was lower than the first day. This finding was not observed in group C in none of the days.

A sudden increase in the mean score of the withdrawal signs and symptoms on the second day is probably due to the consumption of narcotics on the day of admission. As figure 2 shows, there is no interaction between the symptoms (power=0.3, if the number of samples were more, there would be probably interaction between the first and second days).

There was a similar increase in the eighth and ninth days, which is probably due to the start of naltrexone administration.

An overall study of the mean score of withdrawal signs and symptoms during the ten days of detoxification shows the efficacy of gabapentin in the drug quit process.

The results of previous studies on experimental animals are evidence of the efficacy of gabapentin in treating morphine withdrawal syndrome. Andrews et al. carried out a study on the rewarding effect of morphine on two distinct phases namely maintenance and development by the CPP (Conditioned Place Preference) method. They found that gabapentin-like compounds (gabapentin & pregabalin) blocked the development of CPP to morphine and also blocked morphine's effects on dopamine release. These compounds have no intrinsic rewarding properties, and could have some therapeutic uses in the treatment of opioid dependence (25). This shows that gabapentin can decrease reinforcement and withdrawal signs via blocking morphine's effect on dopamine release.

The study performed by Martinez-Raga showed that gabapentin reduces symptomatic medications and had a beneficial effect on the symptoms of heroin withdrawal (26).

Moreover it has been observed that gabapentin is structurally similar to the inhibitory neurotransmitter, gamaaminobutyric acid (GABA) (17), and the action of this drug may be related to the enhanced potentiation of (GABA) inhibitory neurotransmission (27). In other studies, GBP efficacy on the opioid withdrawal syndrome have been reported (19, 20).

Total score of withdrawal signs during the 10 days of treatment

As shown in figure 1, in group G, mean score of withdrawal signs on the second day shows a significant increase comparing to the first day and then it decreases and only once it increases on the ninth day, comparing to the eighth day. Mean score from the eighth day to the tenth day is less than that of the first day.

In group C, there is an increase in the mean score until the third day and then decreases on the fourth day. From the fourth day till the seventh day it shows an increase with a slight draft and decreases from the seventh day. In this group, too, mean score of the last days is even a little higher than the first day.

There are significant differences between the two groups on the sixth day (P=0.023), seventh day (P=0.0001), and eighth day (P=0.003). Interactions of signs in the second day is significant [F(1)=4.071, P=0.04]. This fact shows a significant difference between the two groups with regards to the process of alterations on the first and second days (Figure 1).

Mean total score of withdrawal symptoms during the 10 days of treatment

Mean total score of withdrawal symptoms shows a significant difference during the detoxification period [F(4.588) =4.310, P=0.001]

As could be seen in the figure 2 regarding the withdrawal symptoms, in both groups the second day shows an increase comparing to the first day. In group C this increase continues till the fifth day and then decreases until the eighth day and again it shows a slight increase. While in group G, decrease starts from the second day and only on the fifth and seventh days show a little increase comparing with the preceding days and the tenth day shows a higher score comparing to the nineth day.

A whole comparison of two groups shows lower mean scores for all the days in group G and there are significant differences between the two groups on the fourth day (P=0.046), fifth day (P=0.015), sixth day (P=0.003), seventh day (P=0.035), eighth day (P=0.033) and the ninth day (P=0.002). In group G mean score of the tenth day is lower than the first day, while this was not true for group C.

SCL-90-R

The results of SCL-90-R in group G showed a significant difference between the first and last days of treatment in all scales. Aggressiveness, anxiety, depression, sensitivity in terms of interpersonal relations, obsession and compulsion, somatic complaints, phobia, paranoid thoughts and psychosis on the first and tenth days showed significant difference (P=0.0001).

In group C, depression (P=0.0001), sensitivity in terms of the interpersonal relations (P=0.001) and paranoia (P=0.013) on the first and tenth days showed significant differences.

In both groups, GSI and PSDI showed a significant decrease in the last day of hospitalization, compared to the first day. Only in group G, PST showed a significant decrease in the tenth day compared to the first day (Table 4).

The effect of gabapentin on psychological signs and SCL-90-R is significant in the gabapentin-treated group. All disorders such as depression, aggressiveness, sensitivity to interpersonal relations, phobia, paranoia, obsession and compulsion, anxiety, psychosis, and somatic complaints showed a significant decrease on the discharge day comparing to the admission day. This finding should be explained cautiously, because the two SCL-90-Rs were repeated with an interval of ten days. On the other hand, the mean score of SCL-90 in group C is higher than group G, but this difference is not significant. According to Letterman et al., gabapentin is highly effective in the treatment of some psychiatric disorders such as bipolar disorders, anxiety, behavioral problems and substance-abuse. Moreover, because of having very limited side effects, no need for therapeutic

drug monitoring and minimal pharmacological interactions, it is a very useful drug indeed (17).

Cabras et al. have performed a study about the efficacy, tolerability and safety of gabapentin as an adjunctive drug in the treatment of schizophrenic patients with manic and hypomanic signs. They found that gabapentin is highly effective in treating mania and hypomania in patients with bipolar disorders and schizophrenia. They introduced gabapentin as a well-tolerated and rapidly acting antimanic drug (28).

The results of all these studies as well as the results of the present study suggest that gabapentin, as a drug which causes no dependency, could be used for decreasing the withdrawal syndrome in opioid-dependency and also in treating psychiatric disorders.

Electroencephalogram

In both groups no significant difference between the first and tenth days were seen in the electroencephalogram indices such as wave activity (normal, slight, moderate, severe), CPS (Cycle Per Second), wave type (alpha, beta, delta, and theta) and epileptic tendency (normal, low, high). There was also no significant difference in these indices between the two groups, but there was a significant difference on the first and tenth days in terms of CPS in group C.

Mattia et al. performed a study on patients with focal epilepsy who were resistant to other antiepileptic drugs. They used gabapentin in these patients and observed only an increase in theta relative power. In their study, gabapentin had no effect on ictal and interictal EEG, and it only caused a reduction in seizure occurrence (29). Also in the present study, there was no significant difference between the two groups with regards to the EEG indices such as the rate of abnormal waves, type of waves, CPS and also epileptic tendency.

It should be mentioned that delta waves are pathologic and theta waves are seen naturally in the partial cortex of people less than 15 years old. Beta waves may be present in case of using some drugs. Therefore, any discussion about wave types in our patients before omitting the effective factors is not possible. On the other hand, there was no convulsive disorder in our patients, and this could be the reason of seeing no difference between EEG indices in the two groups.

The exact mechanism of action of gabapentin is not well known, but its significant efficacy in the treatment of withdrawal signs and symptoms and psychiatric disorders during detoxification period can suggest it as one of the main choices in treating the opioid withdrawal syndrome. Further physiological and controlled studies are recommended to determine the potential effect of gabapentin during the detoxification period.

Acknowledgement

Kerman Azad University and Shaheed Beheshti Hospital staffs are acknowledged for their assistance.

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