Beneficial Effects of Rosmarinus Officinalis for Treatment of Opium Withdrawal Syndrome during Addiction Treatment Programs: A Clinical Trial

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Original Article

Abstract

Background: Withdrawal syndrome may influence patient's motivation for participation in addiction treatment programs. Management of the symptoms can improve the success rate of addiction treatment programs. In the present study, we have evaluated the efficiency of an herbal product as adjunct therapy for alleviation of withdrawal syndrome in opium abuse.

Methods: In the present clinical trial, 81 patients were assigned into case and control groups. The control group was treated with methadone and placebo for 4 weeks. The case group was treated with methadone and powdered dried leaves of Rosmarinus officinalis for the same interval. Occurrence of withdrawal syndrome was compared between groups on days 3, 7, and 14 after beginning of the treatment, and the possible signs and symptoms of withdrawal syndrome were checked. The clinical opioid withdrawal scale (COWS) was used for evaluation of withdrawal syndrome in the patients.

Findings: Patients in the case group experienced less severe withdrawal syndrome compared to those in the control group; chiefly bone pain, perspiration, and insomnia.

Conclusion: The present study showed that rosemary can be used as an optional extra drug for treatment of withdrawal syndrome during treatment programs for opium addiction and possibly addiction to other opioids.

Keywords: Withdrawal syndrome, Rosmarinus officinalis, Opium, Addiction

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Introduction

The global epidemic of opiate use continues to spread, especially in developing countries. Research centers have focused on nonaddicting opioids or agents that have the capability to prevent the addiction process; however, the problem has not yet been solved.[1] Opioid withdrawal symptoms consist of dysphoric mood, nausea or vomiting, muscle aches, lacrimation, rhinorrhea, pupil dilation, piloerection, sweating, diarrhea, yawning, fever, and insomnia.[2] Medications that are used to reduce symptoms of opioid withdrawal syndrome have different mechanisms. However, their prescription has its own limitations and side effects.[2] Earlier studies conducted on animals have suggested that Rosmarinus officinalis (rosemary) can be effective in alleviation of symptoms of opioid withdrawal syndrome.[3,4]

Rosemary grows in many parts of the world.[5] It is used fresh, dried, or as essential oil.[6] Chemical content of the plant consists of flavonoids, phenols, volatile oils, and terpenoids.[7] Rosmarinus officinalis acts as antispasmodic, smooth muscles relaxant, memory booster, antioxidant, inducer of neural growth factor, and anti-microbial agent.[5,8-11] It has also been claimed that the plant is effective in treatment of headache, musculoskeletal pains, and seizures.[12-14] Analgesic effects of aqueous and alcoholic extract of Rosmarinus officinalis have been antagonized by naloxone. This may imply its interaction with opioid receptors.[3,4]

Use of Rosmarinus officinalis has been approved as supplemental therapy for dyspepsia.[15] It has been approved for oral use as food supplement in humans by the FDA.[16] The effects of Rosmarinus officinalis on improvement of withdrawal symptoms in morphine dependence have been studied in mice.[3] It has been suggested that it may reduce symptoms of withdrawal syndrome by inducing GABA system.[3] In the present study, we have evaluated the use of rosemary as an herbal drug for treatment of opium withdrawal syndrome.

Methods

The present study which was a randomized clinical trial has been performed in Arak city, Iran. It is registered in IRCT (register number: IRCT138903054033N1). Its details are cited in the website of International Clinical Trials Registry Platform of WHO (http://apps.who.int/trialsearch). It has been approved by the local Ethical Committee of Arak University of Medical Sciences, Arak, Iran.

The patients participated in the study if they had the inclusion criteria. They were selected from drug abusers referred to a rehabilitation clinic of a teaching university hospital. The inclusion criteria were: any form of abuse of opium at least 2.3 grams per day continuously for at least one year, age between 20-50 years, no history of any major medical disease, and no history of sensitivity to the plant. Eighty was determined as the target sample size, as approved by a biostatician.

Half of the patients were randomly assigned as control group. The other half was allocated as case group. The exclusion criteria were failure to follow up, allergy to rosemary, and continued use of opium during the trial.

Both groups were treated by methadone for short-term detoxification. They received 20 mg/day in the 1st week, then 15 mg/day in the 2nd week, followed by 10 mg/day in the 3rd week, and 5 mg/day in the 4th week. The rosemary capsules (filled with dried powdered leaves) had been produced by Barij Essence Pharmaceutical Company, Kashan, Iran, and contained 300 mg dried leaves of Rosemary. They were administrated to the patients in the case group as 16 capsules/day for the first 3 days, 12 capsules/day for the following 4 days, and then 8 capsules for the next week in divided doses. Patients in the control group received placebo produced by the same company. All patients were visited in the 3rd, 7th, and 14th day after starting of the treatment by a physician. The physician and the patients in the case and control groups did not know anything about the content of the capsules and which patient belongs to which group.

The clinical opioid withdrawal scale (COWS) was used for evaluation of withdrawal syndrome in the patients. In addition, sleep duration and insomnia were evaluated in the patients.

The results were compared between the 2 groups using paired t-test. SPSS for Windows (version 11.5; SPSS Inc., Chicago, IL., USA) was used for statistical analysis.

Results

98 patients participated in the study. 17 patients

Table 1. General characteristics of the studied patients

	Case group (n = 39)	Control group (n = 42)	P
Age	36.7 ± 4.58	36.6 ± 7.53	Not significant
Male/female ratio	All were male	All but one were male	Not significant
Mean opium use (gram/day, as stated by the patients)	1.8 ± 0.43	1.7 ± 0.51	Not significant
Mean duration of opium abuse (years, as stated by the patients)	10.1 ± 5.21	10.2 ± 6.08	Not significant

failed to finish their treatment course, mainly due to failure to follow up (9 patients) and continued use of opium (6 patients). General characteristics of the patients have been demonstrated in table 1.

Mean COWS score was 9.2, 7.5, and 6 in the case group in the 3rd, 7th, and 14th days of treatment, respectively. The corresponding scores were, respectively, 12.1, 11.7, and 7.8 in the control group. The differences were statistically significant for the 3rd and 7th days ($P < 0.050$).

There were significant differences between duration of sleep in 3rd and 7th days between case and control groups ($P < 0.001$ and $P < 0.002$, respectively). More details have been displayed in table 2.

Table 2. Mean duration of sleep per day in case and control groups

Group	3rd day (hours)	7th day (hours)	14th day (hours)
Case	6.5	6.9	7.3
Control	5.0	5.5	6.1

Furthermore, as can be seen in table 3, there was significant difference in the percentage of patients who were complaining from insomnia between case and control groups on 3rd and 7th days ($P < 0.001$).

Table 3. Percentage of patients with insomnia in case and control groups after the treatment

Group	3rd day (%)	7th day (%)	14th day (%)
Case	25.0	12.5	15.0
Control	77.5	72.5	20.0

Discussion

Results of the present study confirmed that rosemary can be used as an adjunct therapy for improvement of withdrawal syndrome during addiction treatment programs. Hosseinzadeh et al. have stated that muscle jerks are the main criteria of morphine withdrawal syndrome. In their study performed on rats, it has been suggested that rosemary can reduce muscle jerks produced by morphine withdrawal syndrome.[4] In another study, the effectiveness of aqueous and alcoholic extract of rosemary in reduction of opium withdrawal syndrome in animals has been proved.[3] In the study of Boroushaki et al., the therapeutic effect of rosemary in treating convulsion was evaluated in comparison with phenobarbital. It was verified that all parts of the plant can reduce convulsion in animals.[14] In our study, the effectiveness of rosemary in the improvement of sleep and reduction of insomnia was demonstrated. It is likely that the anticonvulsant effect, found in the former study, occurs with the same mechanism as rosemary's affect on reducing insomnia in the present study. Moreover, it was shown that rosemary can reduce musculoskeletal pain.[13] In the current study, the effectiveness of rosemary in reduction of musculoskeletal pain in opium addicts has also been demonstrated.

In summary, results of the current study reveal that Rosmarinus officinalis can improve opioid withdrawal syndrome to some extent. This can be attributed to various properties of the plant, including anti-inflammatory and psycho-stimulant effects.[17,18] Extraction of alkaloids present in the plant may elucidate true constituents of the alkaloid(s) responsible for this effect.

Conclusion

The present study showed that rosemary can be used as an herbal drug for treatment of withdrawal syndrome during treatment programs for opium addiction and possibly addiction to other opioids.

Conflict of Interests

The Authors have no conflict of interest.

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تأثیر مفید گیاه رزمارینوس افیشینالیس در درمان سندرم محرومیت ناشی از تریاک در برنامه‌های ترک اعتیاد

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مقاله پژوهشی

چکیده

مقدمه: سندرم محرومیت می‌تواند در برنامه‌های درمانی ترک اعتیاد و تمایل بیمار برای مشارکت در آن‌ها اختلال ایجاد کند. کنترل علایم سندرم محرومیت می‌تواند شانس موفقیت در ترک اعتیاد را بهبود بخشد. در این مطالعه اثر یک داروی گیاهی به عنوان داروی مکمل در بهبود علایم سندرم محرومیت ناشی از اعتیاد به تریاک، مورد ارزیابی قرار گرفت.

روش‌ها: در کارآزمایی بالینی حاضر، ۸۱ بیمار در دو گروه مورد و شاهد تحت مطالعه قرار گرفتند. گروه شاهد برای مدت ۴ هفته تحت درمان با متادون و دارونما بودند. گروه مورد برای همین مدت تحت درمان با متادون و کپسول‌های حاوی برگ‌های خشک شده و پودر شده گیاه رزمارینوس افیشینالیس قرار گرفتند. بیماران ۳، ۷ و ۱۴ روز پس از درمان از نظر علایم سندرم محرومیت ارزیابی شدند. برای ارزیابی علایم سندرم محرومیت در بیماران از معیار COWS (Clinical opioid withdrawal scale) استفاده گردید.

یافته‌ها: شدت علایم سندرم محرومیت در گروه مورد به میزان قابل توجهی کمتر از گروه شاهد بود. این تفاوت به ویژه در مورد تعریق، بی‌خوابی و درد استخوانی چشمگیرتر بود.

نتیجه‌گیری: مطالعه حاضر نشان داد که می‌توان از گیاه رزماری به عنوان داروی مکمل جهت کنترل علایم سندرم محرومیت در برنامه‌های درمانی برای ترک تریاک و شاید سایر اپیوئیدها بهره جست.

واژگان کلیدی: سندرم محرومیت، رزمارینوس افیشینالیس، تریاک، اعتیاد

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