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Short communication

Add-on gabapentin in the treatment of opiate withdrawal

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Abstract

Gabapentin is an antiepileptic drug shown to be effective in the treatment of pain disorders and appears to be useful as well for several psychiatric disorders, including bipolar disorder, anxiety disorders, alcohol withdrawal and cocaine dependence. Gabapentin, at a dose of 600 mg three times a day, was evaluated as an add-on medication to a standard detoxification regime in seven heroin dependent individuals undergoing outpatient opiate withdrawal treatment. All seven patients successfully completed opiate detoxification and commenced opiate antagonist treatment with naltrexone on day five of withdrawal treatment, as scheduled. No adverse event was noted. Gabapentin appeared to lead a reduction in symptomatic medication and an overall beneficial effect on symptoms of heroin withdrawal.

Keywords: Detoxification treatment; Gabapentin; Opiate withdrawal

1. Introduction

Pharmacological treatment of opiate withdrawal symptoms is aimed to facilitate a safe transition to a relapse prevention program, while ameliorating signs and symptoms of withdrawal. Alpha-2 adrenergic agonist drugs are the main non-opiate alternative for withdrawal treatment and the preferred option when naltrexone maintenance treatment is to be commenced (Gowing et al., 2002). However, clonidine the only alpha-2 adrenergic agonist available in Spain is associated with high rates of adverse effects, including drowsiness, fatigue lethargy and dry mouth and particularly hypotension. Indeed, outpatient management of opiate withdrawal using clonidine is generally recommended for a restricted number of patients (American Psychiatric Association, 1995).

Gabapentin is an antiepileptic drug shown to be effective as add-on therapy for patients with drug-resistant partial seizures with or without secondary generalization (Marson et al., 2001). Due to its tolerability, and its broad and complex mode of action, gabapentin has also been studied for other indications. The largest area of nonepileptic use of gabapentin is neuropathic pain (Rice and Maton, 2001), but it appears to be effective in other types of pain as well. Indeed, administration of a single dose of gabapentin (1200 mg) has shown to reduce morphine consumption and postoperative pain in patients undergoing radical mastectomy (Dirks et al., 2002). In addition, it has been reported to be a useful pharmacological agent for several psychiatric disorders, such as bipolar disorder, social phobia and other anxiety disorders (Cabras et al., 1999; Pande et al., 1999). A number of studies have also suggested the potential effectiveness of gabapentin in the treatment of alcohol withdrawal (Bonnet et al., 1999; Bozikas et al., 2002) and cocaine dependence (Myrick et al., 2001).

Using the conditioned place preference test in the rat to assess the rewarding properties of morphine, pretreatment with gabapentin and the related compound pregabalin blocked the increase in dopamine in the nucleus accumbens following acute morphine administration, as well as the development of conditioned place preference to morphine (Andrews et al., 2001). Therefore, it was concluded that gabapentin might have some therapeutic use in the treatment of opiate dependence. Interest in antiepileptic agents in the management of opiate withdrawal has led to a double-blind

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pilot study that compared the association of mianserin and carbamazepine with clonidine (Bertschy et al., 1997). The two treatments did not differ in the intensity of the withdrawal. More recently, three patients undergoing an inpatient opiate detoxification program were reported to achieve nearly complete control of withdrawal symptoms using topiramate (Zullino et al., 2002). However, to our knowledge there are no reports of gabapentin in the treatment of opiate dependent patients.

In the present report, co-adjuvant administration of gabapentin was evaluated in seven heroin dependent individuals undergoing outpatient treatment for opiate withdrawal at a specialized outpatient treatment center for the treatment of patients with addictive disorders in Valencia, Spain. The aim was to assess whether symptoms of opiate withdrawal were ameliorated and transition to relapse prevention program with naltrexone was facilitated with gabapentin as an add-on medication to a standard detoxification regime.

2. Methods

2.1. Patient population

The patients included five men and two women (mean age 28.1 years; range 23–33) who met ICD-10 criteria (World Health Organisation, 1992) for opiate dependence for over 2 years and were smoking heroin (“chasing the dragon”) during that time. All patients provided informed consent prior to entering the study. Only one of the patients was occasionally using heroin intravenously. They had taken their last heroin dose within 24 h prior to initiate the detoxification treatment. Patients were reported to be using between 0.5 and 1 g of heroin per day. Four of the patients (three males and one female) had undergone one previous outpatient heroin detoxification treatment at our Unit in the previous 12 months. None of the patients were currently dependent on other substances. However, two of them had a past history of cocaine dependence and two further ones a past history of cocaine abuse. In addition, three patients had a past history of benzodiacepine abuse and four were current occasional cannabis users. All of the patients were smokers (>20 cigarettes per day).

Five of the patients were single, while the remaining two patients were separated. However, all of them were living with a cooperating close relative that acted as an informant to ensure treatment compliance.

2.2. Treatment setting and procedure

The study was conducted at a specialized Addictive Behaviors Unit (Unidad de Conductas Adictivas), an outpatient unit for the treatment of patients with an addictive disorder serving a specific catchment area in the city of Valencia (Spain). On arrival to the Unit, patients are thoroughly assessed prior to deciding the treatment option considered more appropriate for each patient.

In brief, gabapentin at a dose of 600 mg three times a day (without any titration) was associated to a standard detoxification regime using a 9-day course of diazepam and symptomatic medication (ibuprofen, loperamide and metoclopramide) on an as required basis. Diazepam was prescribed at a 60 mg/day dosage (15 mg q.i.d.) for the first 4 days and then reduced by 10 mg/day during the following 5 days. Patients were assessed on the third day after initiating withdrawal treatment and again on day five when induction to naltrexone maintenance was scheduled. The next visit was scheduled for 5 days after commencing naltrexone treatment.

3. Results and discussion

All seven patients successfully completed opiate detoxification and commenced opiate antagonist treatment with naltrexone on day five of withdrawal treatment, as scheduled. Opiate withdrawal is characterized by autonomic hyperactivity, with symptoms such as marked anxiety, intense craving, irritability, insomnia, nausea, diarrhea and muscular pain. It would therefore be expected that patients would require additional doses of diazepam and high doses of analgesic and other symptomatic medications. Indeed, during previous detoxification treatment using the same regime, but without gabapentin, the four patients treated at our Unit had required between 80 and 120 mg (mean daily dose: 105 mg) of diazepam and up to 3000 mg of ibuprofen per day (mean daily dose: 2130 mg) for the 5-day acute detoxification period. In the present case series, however, the average total amount of ibuprofen used during the 5 days detoxification period for the seven patients was 4.9 (range 3–8) tablets (2914 mg; range 1800–4800 mg). None of the patients required additional hypnotic medication, including any extra diazepam doses at nighttime, as confirmed by the supporting relative and by revising the medication box. This may indicate a beneficial effect of gabapentin on symptoms of opiate withdrawal, which may be related to its effects on the gabergic and glutamatergic systems, as well as on its actions on several monoamine neurotransmitters (Taylor et al., 1998). Gabapentin was continued for 2 weeks after initiating naltrexone treatment and then tapered off over a 3-day period.

Mild to moderate dizziness and somnolence, generally transient and confined to the titration phase or first week of treatment are the most common adverse events in the clinical trials with gabapentin (Rice and Maton, 2001). The “sedating” side effects may have contributed to ameliorate some of the symptoms of heroin withdrawal, which may explain why none of our patients reported any adverse events despite the relatively high doses used, without titration in these case series. Furthermore, gabapentin appeared to lead a reduction in symptomatic medication

and an overall beneficial effect on symptoms of heroin withdrawal.

A limitation of the present study was that gabapentin was not administered as monotherapy and consequently it is difficult to understand the actual effect of gabapentin in the management of opiate withdrawal in these group patients that successfully commenced naltrexone maintenance on day five of withdrawal treatment, as scheduled. An additional limitation was that no withdrawal or symptomatic scales were used for measuring symptoms of opiate withdrawal. Future studies would need to consider using objective measures as evidence for the superiority of the treatment over the standard treatment.

4. Conclusion

Considering its tolerability, the relatively good side-effect profile, and lack of significant interactions, together with the results from this report it appears that gabapentin could be a useful pharmacological adjunct in the treatment of opiate withdrawal and deserves further research through well-designed controlled studies.

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