The detoxification treatment for pentazocine addiction

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Abstract

Pentazocine (Fortral®) is an opioid analgesic acting on two types of opioid receptors, its dominant effect being mediated by kappa receptors. The addiction-developing potential of pentazocine is more reduced than that of morphine; the addiction is more frequent among hospital staff or it is doctor-induced. There are several detoxification methods for opioid addiction, among which agonist or opioid-antagonist administration..

Keywords: *pentazocine, kappa receptors, detoxification, agonist/opioid antagonist administration*

Rezumat

Pentazocina (Fortral®) este un analgezic opioid care acţionează asupra a două tipuri de receptori, efectul său dominant fiind mediat de receptorii kappa. Potenţialul de dezvoltare a adicţiei la pentazocină este mai redus decât cel al morfinei; dependenţa este mai frecventă în rândul personalului spitalicesc sau este indusă de medic. Există câteva metode de detoxificare pentru dependenţa de opioide, printre care administrarea unui agonist sau a unui opioid antagonist.

Cuvinte-cheie: *pentazocină, receptori kappa, detoxificare, administrare agonist/opioid antagonist*

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Introduction

Pentazocine (Fortral®) is an opioid analgesic which, unlike morphine, produces its effects by acting on both opioid and kappa receptors. Its main effects are due to the activity of kappa agonists, while the opioid effect upon *miu* receptors is lower. Owing to the partial agonist effect of opioid receptors in morphine addiction, the administration of pentazocine can trigger or precipitate the withdrawal syndrome[1].

Pharmacodynamically, its analgesic effect takes from 3 to 5 hours, has a marked sedative effect and depresses breathing to a lesser degree than morphine. Thirty to sixty mg of pentazocine administered intravenously determines an analgesic effect equal to 10 mg of intravenously adminstered morphine. Therapeutically, as an analgesic, the recommended dose is a 30 mg ampoule administered subcutaneously, intramuscularly or intravenously every 3 or 4 hours.

For intravenous administration, the addiction-developing potential of pentazocine is moderate as compared to that of morphine. Similarly, oral administration has a diminished effect in developing addiction. In Romania, as well as in other countries, the pentazocine addiction cases are recruited mostly among medical staff/personnel or are doctor-induced. The obtaining and the illegal administration of pentazocine are less frequent but possible[3]. The doses used by pentazocine-addicted persons vary from 5 to 20 ampoules/day, administered intravenously.

The classic treatment of psychoactive substances addiction consists of two stages: the withdrawal treatment (detoxification) and the long-term treatment of the addiction itself.

The pentazocine withdrawal syndrome

According to DSM-IV, the diagnostic criteria for the opioid-withdrawal syndrome are the following:

A. Any of the following situations: 1. interruption or reduction of opioid administration after a prolonged period of use (several weeks or more) in large doses; 2. administration of an opioid-receptors antagonist after an interval of opioid use.

B. Three or more from the following symptoms setting in a few minutes up to several days after the situations mentioned at A.: irritability; nausea or vomiting; muscular aches; eye watering or rhinoroea; pupil dilatation; hair erection or perspiration; diarrhea; coordination disorder; fever; insomnia.

C. The symptoms from B determine a significantly distressed or deteriorated condition during social, professional or other types of activities.

D. The symptoms are not caused by a general health condition and cannot be attributed to another mental disorder.

The withdrawal from opioids acting partly as kappa receptor agonists, a class to which pentazocine belongs, sets in quickly, whereas symptoms decrease and only take a few days.

The clinical description has several elements in common with or is partly similar to the opioid-agonist withdrawal syndrome, but there are also distinct features. For instance, the withdrawal from opioids with exclusive action on kappa receptors does not cause behavior modifications known as craving. The presence of these manifestations in pentazocine withdrawal is an argument in favor of pentazocine action on *miu* receptors[1].

The detoxification treatment

So far, there have been three main wide-scale used detoxification methods for opioid-addicted patients: the substitution treatment with long-term effect opioids administered orally; the treatment with alpha-2 adrenergic agents associated or not with opioid antagonists; ultrarapid/detoxification.

The substitution treatment

In the treatment of agonist-opioid withdrawal, the most frequently used method is the methadone substitution. Since methadone has only *miu*-agonist effects, its administration affects only some of the pentazocine withdrawal symptoms, the latter being only partially improved[1,8].

Recently, other long-term acting/long-lasting *miu*-agonist substances have been used as substitution treatment. As to a better control on withdrawal symptoms, good results have been obtained by the administration of buprenorphine, a treatment that has been also introduced lately in current practice[7]. Another *miu*-agonist studied recently is the levo-methadilacetate, with a longer effect than that of methadone and buprenorphine. Although the findings communicated are good, this drug is not widely used, even though its administration is accepted in medical practice[5]. In the treatment of pentazocine withdrawal, both buprenorphine and levo-methadilacetate show the same disadvantages as methadone – i.e., the exclusive *miu*-agonist effect.

The detoxification treatment with non-opioid agents

Clonidine, an alpha-2 adrenergic receptor agonist, originally used to lower high blood pressure, has been proven to diminish some of the opioid-withdrawal symptoms. In the case of pentazocine addiction, due to the relatively low intensity of withdrawal symptoms as compared with those caused by the interruption of other opioid substances administration, the sudden interruption of pentazocine and the subsequent administration of clonidine are the most recommended therapeutic solution. Clonidine is administered three times per day, in 0.1-0.3 mg doses. In the case of outpatients, the administration of doses higher than 1 mg/day is not recommended even though inpatients could take up to 2.5 mg/day doses. The main side effect of clonidine is the lowering of blood pressure, which can be extreme. Clonidine administration allows the shortening of the detoxification period for inpatients as compared with the time interval needed for the substitution treatment consisting of the gradual decrease of doses. However, clonidine has only little effect on muscular aches, lethargy, insomnia and craving, which continue long after the proper withdrawal. Similarly, there are no data to support a decrease of the relapse rate in patients treated with clonidine[3,6].

Another alpha-2 adrenergic agonist is lofexidine. It is used for opioid withdrawal treatment and, similarly, improves the symptoms. Even though in the United States of America its administration is forbidden, it has replaced clonidine in Great Britain because of its less marked effect on blood pressure[6].

In some cases, a more visible amelioration of opioid withdrawal symptoms has been noticed in the case of associating diazepam to alpha-2 adrenergic-agonists, with the effect of shortening the withdrawal time and a faster introduction of opioid-receptor antagonists such as naltrexone. This treatment causes a complete detoxification in less than 5 days, with the administration of naltrexone one day after the setting in of the withdrawal stage and the beginning of alpha-2 adrenergic agents therapy[4,6].

The ultrarapid detoxification

The duration of the critical opioid withdrawal stage can be significantly shortened by using opioid-receptor antagonists, causing the agonists to mobilize on the receptors' level. Consequently, the withdrawal syndrome is more intense than the one subsequent to the sudden interruption of opioid administration. Therefore, attempts have been made to administer opioid-receptor antagonists associated with clonidine in order to lower the intensity of the withdrawal symptoms. There are reports on cases in which the association of sedatives to the clonidine-naltrexone treatment determines an increased control on the withdrawal symptoms[3].

There have also been reports on the duration of detoxification being shortened to less than two days by the administration of opioid-receptor antagonists during several hours of complete/thorough anesthesia. The basic technique known as ultrafast detoxification consists in the administration of premedication targeted on reducing vomiting and intestinal peristalses such as sandostatin or cimetidine, followed by the administration of neurovegetative/modulators such as clonidine. The patient is then intubated and anesthetized with midazolame or tiopenthal. Naltrexone is administered by naso-gastric probe. Anesthesia takes from 4 to 8 hours. Although some patients show typical but low intensity withdrawal symptoms on wakening, the majority experience a general discomfort which persists 24 to 48 hours. Immediately after recovery from anesthesia, the naltrexone therapy is initiated[2]. Several solutions have been proposed by replacing premedication, intravenous administration of naloxon or the usage of other anesthetics.

This technique has been used for the interruption of the substitution treatment with methadone or buprenorphine. Also, in this case, ultrafast detoxification has been realized on the background of intense sedation without intubation or naso-gastric probing[2,6].

There are few certain data on cases in which this detoxification method was used. Similarly, there are not solid proofs to sustain the increased effectiveness of this technique as compared with a 4 to 10 days of detoxification.

Methodology

Between September 2002 and September 2003, we enrolled a number of eleven inpatients from the Clinic of Psychiatry III for a detoxification treatment for pentazocine addiction.

As a method for evaluating the therapy efficiency, we performed toxicology control analyses in the Forensic Institute in Cluj-Napoca.

Results

A couple of therapy methods were performed for the eleven inpatients, but we applied a common principle, that is the complete withdrawal from pentazocine.

We used the following types of medicines:

- alpha-2 adrenolitics
- opioid-receptor antagonists: nalorphine, naloxone
- anticonvulsants with ortotimic effect
- clasic and novel neuroleptics
- antidepressants: tricyclics and SSRIs
- miscellaneous: vitamines, antibiotics and glucose perfusions.

Under the circumstances of the complete stopping of pentazocine, the most effective way from a therapeutic point of view consisted in clonidine administration, 0.15 mg per day, together with opioid antagonists. We used either nalorphine 2 ml (5 mg) divided into two equal dosages daily, i.v. or i.m., or naloxone, one ampoule/day.

Another positive therapeutic method consisted in: alpha-2 adrenolitics administered in order to reduce the intensity of withdrawal syndrome (clonidine 0.15 mg/day) associated with a sedative neuroleptic (tiapridal ampoule or tablets) 300 mg daily, up to maximum 600 mg daily.

As an associated treatment, we used antidepressive medication. We had three cases in which we could notice depressive symptoms associated to withdrawal syndrome.

Conclusions

Pentazocine (Fortral®) is an opioid analgesic acting on two types of opioid receptors, its dominant effect being mediated by kappa receptors. The addiction-developing potential of pentazocine is more reduced than that of morphine; the addiction is frequent among hospital staff or it is doctor-induced.

There are three main detoxification methods for opioid addiction:

1. The most recommended therapeutic method consisted in the sudden interruption of pentazocine administration with alpha-2 adrenolitics administered in order to reduce the intensity of withdrawal syndrome associated with a sedative neuroleptic (tiapridal).

2. In order to reduce the detoxification period in severe opioid addiction, the administration of opioid-receptor antagonists (nalorphine, naloxone) associated with clonidine prescription is recommended.

3. The third method of treatment, that could not be applied in our clinic, consists in the ultrarapid detoxification. With this method, it is induced the withdrawal syndrom by administrating opioid-receptor antagonists and after premedication the patients are intubated and anesthesized. Naltrexone is administered by naso-gastric probe, followed by clonidine. ■

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