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Addiction to Nefopam: A Rare and Poorly Documented Clinical Entity in Sub-Saharan Africa

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Abstract **Case Report**

Addictions represent a major public health problem in developing countries, with health, economic and socio-professional impacts. The consumption of psychoactive drugs is responsible in France for more than 100,000 preventable deaths per year [1]. Data from epidemiological surveys on the gravity of the situation in sub-Saharan Africa are essentially hospital-based and not very representative of reality, because there are few services specializing in addictions. Opioid analgesics are molecules whose addictogenic potential has been known and described for many years [2]. In Cameroon, non-morphine analgesics are widely prescribed for the treatment of pain. Addiction to long-term use of non-opioid analgesics remains anecdotal in the scientific literature. We report here a rare case of addiction to Nefopam, a non-opioid analgesic, in a 45-year-old black woman with fibromyalgia. The aim of this presentation is to draw the attention of clinicians to the risk of addiction linked to the misuse of nefopam.

Keywords: Addiction, Nefopam, Essos Hospital Center.

INTRODUCTION

Addictions are a major public health problem in developing countries, with health, economic and socio-professional impacts. The consumption of psychoactive drugs is responsible in France for more than 100,000 preventable deaths per year [1]. The data from epidemiological surveys on the gravity of the situation in sub-Saharan Africa are those collected in hospitals, and they are not representative of reality, because there are no services specializing in addictions. Opioids are molecules whose addictogenic potential is known and documented [2]. Fibromyalgia is one of the most important chronic pain conditions, with a prevalence of 2-4% in the general population and a ratio of 3.5% women to 0.5% men [3, 4]. The pain generated by this clinical entity is the cause of physical and psychological discomfort, and promotes overuse of analgesics. Addiction to long-term use of non-opioid analgesics is anecdotal in the scientific literature [5]. We report here a rare case of addiction to nefopam, a centrally acting non-opioid analgesic, in a 45-year-old black woman with fibromyalgia. The interest of this presentation is to draw the attention of clinicians to the risk of addiction, linked to the misuse of this molecule.

CASE REPORT

This is a 45-year-old woman, an intensive care nurse. She suffered from fibromyalgia since the age of 30. She does not consume alcohol or tobacco. The anamnesis does not find a psychiatric history, and a consumption of psychoactive substances. She has a normal body mass index. The basic treatment of his pathology is based on oral administration of Duloxetine 60 mg per day, combined with relaxation exercises. Her doctor prescribed 20 mg of nefopam intramuscularly, three times a day, for a painful attack. The use of this molecule for ten years has led to a gradual increase in doses to relieve pain. She uses unconventional measures to obtain the drug. She self-administers supra-therapeutic doses of this drug intravenously, 500mg (25 ampoules) per day. She claims that this dose gives her

an intense feeling of physical and psychological well-being.

All the weaning attempts initiated over the past five years have been unsuccessful. this failure is characterized by violent behavior, aggression, finger tremor and excessive sweating. During his last hospitalization, a decreasing dose schedule of nefopam was started by the resuscitator in combination with the administration of low doses of oral clonidine (at a dose of 0.1 mg every 6 hours). Withdrawal of nefopam was obtained after 5 weeks of follow-up. But we observed a relapse, and attempts to manipulate the nursing staff to obtain nefopam. The patient was offered a combination of clonidine, music therapy sessions and relaxation techniques. Discharge was authorized upon obtaining complete weaning, after a hospital stay of 12 weeks.

DISCUSSION

The International Association for the Study of Pain defines pain as "an unpleasant feeling and emotional experience in response to or described in actual or potential tissue damage" [6]. There are two types of pain: pain due to excess nociception and neuropathic pain. The pain induced by fibromyalgia is neuropathic pain. It is pain associated with injury or disease affecting the somatosensory system [7]. Its treatment uses co-analgesics, the main ones being antidepressants, corticosteroids, and NMDA receptor antagonists (N-methyl-D-aspartate). Nefopam is a special type WHO level 1 analgesic. It has antinociceptive and antihyperalgesic properties with a mechanism of action that is not yet fully understood [8]. It is indeed a central pain reliever, not an opioid drug. Nefopam appeared in the 1960s [9]. Ten years later, he found a therapeutic indication in the management of pain due to excess nociception, specifically postoperative pain [10]. The prescription of nefopam for the treatment of pain has seen renewed interest in recent years around the world and particularly in sub-Saharan Africa. This finding remains theoretical in countries with low per capita income, due to the poor documentation due to the absence of addictovigilance centers. The French Medicines Agency reported in May 2020 111 notifications of nefopam addiction reported to French addiction monitoring centers, with an average daily dose of 14 ampoules. 64% of patients injected nefopam. Almost 40% of patients obtained it illegally. These statistics suggest that nefopam addiction is a real clinical entity, the gravity of the situation no longer to be overlooked. it deserves to be taken into account by clinicians and government policies in order to prevent and stem this trend. Indeed, the sales volume of nefopam has continued to grow since its marketing in 1983 [11, 12]. Nefopam exposes people to a theoretical risk of dependence [13, 14] and to abuse, probably due to its psychostimulant properties [14, 15]. In Cameroon, only the injectable form of 20mg / 2ml is marketed. Nefopam is believed to inhibit the reuptake of norepinephrine, serotonin and dopamine. A recent hypothesis advances NMDA antagonist properties [16, 17]. It also has marked atropine properties [18]. The main side effects of nefopam are atropine effects. Hypersensitivity reactions, severe neuropsychic disorders are reported [18]. From a medical point of view, addictions are brain pathologies defined by dependence on a substance or activity, with deleterious consequences [19, 20]. The diagnosis of addiction is based on criteria defined and set by international mental health bodies and listed in a manual, the “Diagnostic and Statistical manual of Mental disorders” (DSM), the fifth edition of which dates from 2013 (Table-1). In our case, it was found: the urgent and irrepressible need to consume nefopam, loss of self-control, addiction, the presence of a withdrawal syndrome, the interference of nefopam consumption on professional activities , the continuation of consumption despite the awareness of the disorders it causes. It was indeed a severe addiction.

Table 1: DSM V diagnostic criteria (source: Diagnostic and statistical manuel of mental disorders, Fifth edition, Copyright © 2013 American Psychiatric Association)

The 11 DSM V diagnostic criteria of the American Psychiatric Association
1-Compelling and irrepressible need to consume the substance or to gamble (craving)
2-Loss of control over the amount and time spent taking drugs or playing
3-A lot of time spent searching for substances or playing games
3-Increased tolerance to the addictive product
5-Presence of a withdrawal syndrome, that is to say all the symptoms caused by suddenly stopping consumption or gambling
6-Inability to fulfill important obligations
7-Use even when there is a physical risk
8-Personal or social problems
9-Persistent desire or efforts to reduce doses or activity
10-Reduced activities in favor of consumption or gambling
11-Continued use despite physical or psychological damage

Note:

- Presence of 2 to 3 criteria: low addiction
- Presence of 4 to 5 criteria: moderate addiction
- Presence of 6 or more criteria: severe addiction

The harmful effects of nefopam are better known and established than its mechanism of action and its therapeutic efficacy. It is likely that the patient felt better overall on nefopam in the context of chronic pain, in part, due to its psychostimulant properties. These would expose to abuse with the development of dependence even in patients without a history. It should be noted that even at recommended doses, the side effects of nefopam can be serious. The use of nefopam should be justified, of very short duration, in patients informed of uncertainties and adverse effects.

CONCLUSION

Abuse of Nefopam may lead to psychostimulant effects, linked to its dopamine inhibiting properties. Nefopam addiction remains a rare and potentially harmful clinical entity. A rational, reasoned and controlled prescription of nefopam would prevent the risk of addiction linked to this molecule. Health policies in sub-Saharan Africa would benefit from implementing addictovigilance networks with the aim of monitoring all psychoactive substances with potential for abuse, including drugs, other legal and illegal substances such as new psychoactive substances (nefopam) and their health consequences in humans.

Contribution of the Authors

All authors contributed to the realisation of typescript. All authors contributed to the behaviour of this job. All authors also declare to have read and approved the finished version of the typescript.

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