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Case Report

Addiction to Nefopam: A Case Report

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Abstract

Introduction: Chronic non-cancer pain is a major public health issue. Analgesics are widely prescribed to provide relief to patients. Misusing these medications or their long-term use may be harmful.

Objective: To report one case of addiction to nefopam, a non opioid analgesic

Observation: A 50 year-old physician woman, with history of celiac disease in childhood, depression, anorexia nervosa, dependence to benzodiazepine, carbamate and buprenorphine, osteoporosis and scoliosis was prescribed nefopam by intramuscular route for relieving back pain twelve years ago. She developed dependence to nefopam and reported depressive symptoms when attempting withdrawal. Nefopam consumption reached 600 mg per day. Numerous medications were attempted, with no improvement of patient's state. Symptoms as manipulation, sex proposals with patients, requesting money to families of patients, a poor speech, blank stare, memory impairment and suicidal thoughts were noticed. During one period of nefopam abstinence, patient displayed geophagia. When withdrawal was obtained, she started tobacco consumption and became dependent to tobacco.

Discussion: The patient meets DSM V criteria for nefopam substance use disorder. Few cases have been reported. Painful diseases are usually associated with nefopam substance use disorder. Amygdala's system and nefopam psychostimulant effect may be involved in dependence behavior.

Conclusion: Prescription of analgesics in patients with chronic pain may require caution. Physicians, pharmacists and patients should be informed about risks related to nefopam. Non pharmacologic treatments and other non opioid medications should be promoted and integrated in multimodal and multidisciplinary care management to provide a biopsychosocial intervention.

INTRODUCTION

Chronic non-cancer pain is a major public health issue and analgesics are widely prescribed to provide relief to patients. Evidence suggested that these medications may be effective in treating acute pain but misusing these medications or their long-term use may be harmful. Indeed, risks of dependence, overdose and death are well-established. With regards to opioid medications for instance, in the United States, abuse or dependence concerned 1.9 million people in 2013 and the prevalence of dependence has been estimated to be 3 to 26% in general medical settings [1]; deaths due to infections (among users by injection) are estimated to be 1.5 to 2% per year (fifth edition of Diagnostic and Statistical Manual of Mental Disorders, DSM V) and cardiovascular, endocrinologic damages, traffic accidents [1], functioning and social issues and financial costs [2] are reported as well.

We aimed to report one case of addiction to nefopam, a non opioid analgesic, to illustrate issues related to chronic pain medications. Indeed, clinicians usually have to treat patients with chronic non-cancer pain and may have difficulties to manage such medications because of risks inherent to these prescriptions.

OBSERVATION

A 50 year-old physician woman, with a history of celiac disease in childhood, depression since she was 22 years old, anorexia nervosa, osteoporosis and scoliosis was prescribed nefopam by intramuscular route for relieving back pain twelve years ago (20 mg to 40 mg per day). She then had been hospitalized twice for benzodiazepine, carbamate and opiod analgesic (buprenorphine) dependence. The patient was sent by her psychiatrist to our addiction medicine department in January 2014; at that time, she prescribed nefopam for herself as she was physician and injected herself 25 vials 20 mg/2 ml of nefopam per day for its psychostimulant effect. She was totally unaware of her dependence to nefopam but accepted to attend regularly

our services. A decreasing schema of the doses of nefopam was started and withdrawal was obtained after 2 months of follow-up. However, she very often relapsed. She reported depressive symptoms when attempting withdrawal. Family's members of the patient reported a history of geophagia during one period of abstinence.

Her nefopam consumption then reached 30 vials per day, i.e. was estimated to be 600 mg per day. Hence, the patient was hospitalized in our department in February 2015. Numerous medications were attempted, with no improvement of patient's symptoms: clomipramine, maprotiline, mianserine, escitalopram, clorazepate, prazepam, zolpidem, olanzapine, levomepromazine; the patient remained unstable, presenting insomnia, anxiety and depressive symptoms. Sedation was finally obtained with quetiapine and decreasing nefopam consumption was restarted.

During the hospitalization unit, medical staff noticed behavioral disturbances as manipulation, sex proposals with patients, requesting money to families of patients and suicidal thoughts. Physicians as well noted a poor speech, blank stare and memory impairment. Nefopam withdrawal was obtained then patient started consuming tobacco (6 cigarettes per day). The patient left the hospital against medical advice, before a diagnosis was made. She then stopped working and increased tobacco consumption, leading to tobacco dependence. Currently, the patient is lost from sight since May 2015.

DISCUSSION

The diagnosis of our patient is not yet clear. She displayed various major depressive episodes since she was 22 years old, eating disorder (anorexia nervosa) and geophagia, numerous substance use disorders, drug changing during the time (benzodiazepine, carbamate, buprenorphine, nefopam, tobacco), poor psychosocial functioning, manipulative behavior, desinhibition (requesting money to families, sex proposals with patients) and cognitive impairement. Bipolar or a psychosis disorder may be suspected but this clinical presentation is atypical.

The patient meets DSM V criteria for nefopam substance use disorder. Very few cases have been reported and patients were usually treated for painful diseases (Table 1). In this case, our patient was initially prescribed nefopam for back pain related to osteoporosis and scoliosis then she developed addiction to nefopam. Maladaptive responses to stress have been observed in patients with long term use of opioids, another kind of analgesics, in the state of withdrawal. Same dysfunctions were observed in patients with chronic pain. Evidence suggested that they share common stress related neurobiologic characteristics in amygdala's neural network that make them more sensitive

Table 1: Reported cases of nefopam substance use disorder.

Study	Gender	Age (years)	Dose (mg)	Duration	Route of administration	Medical/ psychiatric comorbidities	Comorbid addictions	Complications - side effets	Sought Effect	Withdrawal syndrome
1. Spadari et al., 2001(6)	F	35	1000	10 years	IM (± IV)	Frontal migraines associated with vomiting since childhood, Anxiodepressive syndrome	Tobacco (10 cigarettes per day)	Deterioration of general condition, many deep abcesses (thighs), bilateral quadriceps pyomyositis, lichenified eczema (legs)	Antidepressant ?	Vomiting recrudescence relieved by conventional antiemetic
2. Bismuth et al., 1987(7)	M	40	80	2 years	Not specified	History of right hemicolectomy for crohn's disease, 5 trauma of long bones, fracture of 5 ribs, numerous attacks of renal colic, 2 gastric ulcers, abscesses of the right buttock, prostatitis, hypochondria, depression	-	Social functioning disability	Antidepressant ?	Not Attempted (patient refused attempting withdrawal)
3. Villier and Mallaret, 2002 (4)	F	42	300-480	10 years	IM	Migraine since the age of 15, depression		Anticholinergic effects (dry mouth and nausea), abscesses in the sites of injection requiring several surgical interventions	To relieve dysphoria, fatigue and psychomotor retardation	Depressive syndrome
	F	40	120	Several years	IM	Congenital osteoporosis with severe blow of knees, anxiety		Tremor, involuntary movement, agressivity and dry mouth, abscesses at the site of injection		Depressive syndrome, dysphoria, fatigue and psychomotor retardation
	M	33	1840	5 months	IV	Ileostomy after an abdominal surgery complication, with implantable drug delivery system	Alcohol and benzodiazepine dependence	Violent behavior, facial dysesthesia and myoclonus, tremor of fingers, and sweating		Not attempted

4. Lin et al., 2010 (8)	M	44	120	1 year	IV (femoral)	Psychosis induced by amphetamine and heroin, insomnia and headaches.	Amphetamine and heroin dependence (free for more than 1 year), Diphenhydramine (started at the age of 43)	Psychosis related to simultaneous dependence on diphenhydramine and nefopam, persisting delirium after discontinuation.		Persisting delirium (visual hallucinations, disorientation and consciousness fluctuations, agitation) after discontinuation sweating, worsening agitation and insomnia

F: Female; M: Male; IM: Intramuscular Route; IV: Intravenous Route
"Age" column indicates the age of patient when diagnostic of nefopam substance use disorder is made. "Duration" column indicates the time the patient has been misusing nefopam.

to stress, experience negative emotions and make them seek opioids and relapse [3]. Research is needed to know whether same mechanisms are involved in case of addiction to nefopam. Moreover, our patient later was seeking nefopam for its psychostimulant effect and not for the analgesic one. That may be another explanation for relapses; indeed, a depressive withdrawal syndrome has been observed and antidepressant and psychostimulant effects of nefopam have been reported [4]. These effects may be related to properties of nefopam as a reuptake inhibitor of serotonin, dopamine and norepinephrine.

Our patient developed dependences regarding many kinds of substances. Cases of poly substance use disorders with nefopam were reported but substances usually shared pharmacological and functional similarities, suggesting cross dependences. In the case of our patient, the substances abused belong to distinct pharmacological categories, so it seems unlikely to be a cross dependence. Moreover, the substances used have very often changed during time, starting with benzodiazepine, carbamate, buprenorphine, then nefopam and recently tobacco. This substance use behavior is striking as well. This suggests a specific individual vulnerability. More research is required to explain pharmacologic bases of such dependence behavior.

The prescription of analgesics agents to treat patients with chronic pain may require caution, given the high risk of dependence in this category of patients [5]. Involvement of pain services and treating comorbid conditions [5], non pharmacologic (Cognitive Behavioral Therapy CBT, exercise therapy) and other non opioid pharmacologic treatments (acetaminophen, non steroidal anti-inflammatory drugs, anticonvulsivants, antidepressants) should be promoted and integrated in a multimodal and multidisciplinary care management [1] to tailor adaptive treatment for each patient and provide a biopsychosocial intervention [3]. Research should aim to develop analgesics with lower abuse liability [3]. The management of pain condition is essential since it influences the prognosis of patients [5]. Medication-assisted therapy (methadone and buprenorphine) seems promising, especially when combined with psychosocial therapies [1].

CONCLUSION

Physicians, pharmacists and patients should be informed about risks related to analgesics. Guidelines for the prescription of these medications in chronic pain should be followed [1] and clinicians should always consider the balance benefit-risk and identify patients at high risk of dependence (history of substance use disorder)

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REFERENCES

1. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain--United States, 2016. JAMA. 2016; 315: 1624-1645.
2. Gouvernement du Canada SC. Votre santé et vous. Analgésiques opioïdes. Disponible Sur. 2009.
3. Ghitza UE. Overlapping Mechanisms of Stress-Induced Relapse to Opioid Use Disorder and Chronic Pain: Clinical Implications. Front Psychiatry. 2016; 7: 80.
4. Villier C, Mallaret MP. Nefopam abuse. Ann Pharmacother. 2002; 36: 1564-1566.
5. Dennis BB, Bawor M, Naji L, Chan CK, Varenbut J, Paul J, et al. Impact of Chronic Pain on Treatment Prognosis for Patients with Opioid Use Disorder: A Systematic Review and Meta-analysis. Subst Abuse Res Treat. 2015; 9: 59-80.
6. Spadari M, Tissot-Dupont H, Tichadou L, Arditti J, Jouglard J, David JM, et al. [Pharmacologic dependence on nefopam (Acupan): a case report]. Thérapie Avr. 2001; 56: 191-193.
7. Bismuth C, Fournier PE, Bavoux E, Husson O, Lafon D. [Chronic abuse of the analgesic nefopam (Acupan)]. J Toxicol Clin Expérimentale. 1987; 7: 343-346.
8. Lin KH, Chen YJ, Wei CF, Yen MH, Hsueh WC, Liao KC, et al. Prolonged withdrawal delirium in concomitant diphenhydramine and nefopam dependence: A case report. Prog Neuropsychopharmacol Biol Psychiatry. 2010; 34: 705-706.

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