



RESEARCH ARTICLE

Iatrogenic Addiction Caused by Meperidine

José Tinoco-Gonzalez*

Digestive Surgery Department, University Hospital Virgen del Rocío, Spain

*Corresponding author: José Tinoco-Gonzalez, Ph.D, Digestive Surgery Department, University Hospital Virgen del Rocío, Spain, E-mail: tinoko243@hotmail.com

Introduction

The meperidine or pethidine was for the first time synthesized in 1939 as an anticholinergic agent, but soon its analgesic properties were discovered [1].

In the first performed studies it was published that the pethidine would mean an alternative to the morphine which would avoid the complications of the use of this like breath depression, constipation, urinary retention, and the potential to produce chemical dependency [2]. The early clinical experience intensified the enthusiasm for this opioid analgesic. The first clinical reports reflect such therapeutic enthusiasm for this new analgesic.

The meperidine came out to the market in 50 or 100 mg dose for subcutaneous puncture, just like in 50 mg/ml solution in 2 ml ampoules and 30 ml vials which made the calculus of the dose and its use very comfortable. This ease of administration caused it quickly became in one of the most widely used analgesic in the treatment of moderated to severe pain.

Material and Methods

We present the case of a 46-years-old patient, taxi driver, derivated to the general and digestive surgery service facing the show up of a 8 × 8 cm suprapubic eventration, secondary to a symphysio plastia made up 20 years earlier, consequence of a symphysiotomy during the vaginal birth, with 15 posterior interventions in order to repair the superior pelvic ring with necessity of affix with plates and screws; causing chronic pain with necessity of implanting neurostimulator, neuropsychological support and handling for the Clinical Unit of pain. In the postoperative period of the hernioplasty with polypropylene mesh, it develops a bad control

pain with analgesic as first step, requiring pethidine support. Progressively the patient was requiring higher doses of pethidine until she required 150 mg/4 h of pethidine with additional rescue dose, keeping this requirement for 80 days. Facing the marked dependence to the medicine it was possible to convert successfully to methadone (30 mg/8 h) so it could be handled in residence with such medicine. During the administration of pethidine, the patient developed edema in lower limbs, rough skin, irrigation deficit, delay in the cicatrization healing, immunodepression, making dehiscence conditional to surgical wound with necessity of implanting vacuum system CAV. The iatrogenic addiction for this, in long term belongs to the possible complications in its use, but it has been documented rarely. With this article we resolve to evidence the effects of the chronic use of a patient, and how prescriptive by a physician bad treatment can lead to iatrogenic dependence on a patient.

Discussion

The chronic opioid administration leads to a pharmacologic phenomenon of progressive sensitivity and decrease of opiate receptors as Jing-Gen Liu, makes reference et al. [3]. This process means clinically in a progressive dependence state B means of which the patient requires progressively more doses in less time interval in between to keep the same effects as it happened to our patient during her admission. Abstinence symptoms were associated to a progressive increase of demonstrated pain by means of pain scale, general state affectation with anxiety, tachycardia and hypertension together with a sudden change in the patient condition who shifted between a negotiation and entreaty position to demanding and aggressive attitude.



Citation: Tinoco-Gonzalez J (2018) Iatrogenic Addiction Caused by Meperidine. Int Arch Addict Res Med 4:027. doi.org/10.23937/2474-3631/1510027

Accepted: June 20, 2018; **Published:** June 22, 2018

Copyright: © 2018 Tinoco-Gonzalez J. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

This term which receives this dependence situation associated to a determinate medical prescription is called "iatrogenic opioid dependence" IOD [4] and it happens more frequently in patients who have a non-controlled pain without an etiologic diagnosis [5].

Eisendrath, et al. [6] confirmed that meperidine became the most used in the United States most used opioid analgesic, prescribed by approximately 60% of the doctors for the acute pain and a 22% for the chronic pain.

In our field, it is applied widely in the clinic practice to relieve the pain caused by cancer or the severe surgical conditions. Despite the clinic guides to control the chronic pain, the availability of many other more adequate opioid, and the vigilance of the governmental authorities, the prescription of meperidine is still usual.

Meperidine is metabolized in the body by two different procedures. The first and predominant is the hepatic metabolism of carboxylesterase meperidine acid, an inactive metabolite. The clinically meaningful procedure is the N-Demethylation by the liver's cytochrome P-450 to normeperidine, an active non-opioid metabolite. This metabolic process is conducted in the microsomal hydroxylation enzyme system. The active metabolite non-opioid normeperidine is neurotoxic and with the half of meperidine's analgesic power, but from double to three times the power as an excitatory agent of the central nervous system. One of the characteristics of the normeperidine accumulation is the tendency of creating anxiety, hyperreflexia, myoclonus, convulsions and mood swings in between the first 24 hours. In our case, the patient presented several episodes of aggressiveness, anxiety, and mood alterations which required psychiatric handling.

If we revise the secondary effects profile and the meperidine/normeperidine combined effect presented in the literature, they contrast with the use performed of itself, the selection process of the analgesic drug has not been the correct. Gaensler, et al. [7] was the first to state that meperidine seemed to have a spasmogenic effect defined to the biliary tract and could cause typical biliary colic, at the same time Murphree [8] claimed that meperidine causes spasm in the smooth muscles. Therefore, we determinate it causes a similar effect on the smooth muscle to the other opioids at a same dose, not being preferential its use in patients with biliary duct pathology in spite of the deep-rooted beliefs of many doctors.

Having in account the current drug verifying system and the utility of the yellow cards to report the adverse symptoms of the already traded drugs, it is curious to note that pethidine does not have a restricted use in our centers yet. According to our center pain control team's experience, its use is advised against even in the narrow margin of patients whom the incredible dependence generated could be indicated. Meperidine has a

very narrow spectrum indicator in our general surgery service, for patients who present an uncontrolled acute pain after the surgery and in any case with a lower use than 48 hours.

The anticholinergic effect produces diminution of the amount of secretion therefore its use has been proven for diagnosis procedures on upper digestive tracks or during difficult intubations. At the same time, there are studies which report its utility for the treatment of the migraine, but due to the addictive factor and some signs of pain flare-up, it is been determined, in long term, an increment of the emergency episodes in this drug, not being necessarily the referential drug for this pathology.

The potential abuse of pethidine was reported by Mather and Meffin [9], who compared its effects with morphine's. Despite the addicted in the streets rarely make use of the pethidine, being a hospital setting drug it is dangerous for some patients and doctors, who had access to this restricted and addictive substance. The patient in our case presented a usual access to such drug by means of the hospital emergency service without a clinical registration which could let us evaluate the accumulated dose of pethidine with an almost daily frequency to the emergency service. Pethidine has been denominated as the "Doctors and Nurses drug", in a United States psychiatric hospital's study, of the total pethidine addicted patients, 65% of the admitted were classified as workers of the health field. This study analyzes the for 5 years the addiction to drugs between Quebec doctors which concludes that the 56% prefer meperidine against 38% who prefer morphine. This fact is even a major problem when instead of being a doctor or a nurse who self-administrates this drug, is the patient that, as a result of a chronic pain receives a drug which develops an almost uncontrollable addiction. In our case, the patient did not belong to the sanitary sphere, but, as it was previously told, she had an easy and usual access to the drug.

The quick start initially exposed as an advantage, makes the drug to be prone to the abuse. Meperidine has a relatively short-time action, (2-5 hours), which makes necessary the repeated dose for the continuous pain control. In our average, the idiosyncrasy of the emergency service makes, as in our case, the use of this drug facing a patient who calls for it as the unique effective therapeutic weapon, and in the emergency context, it is usually administrated if this measure fixes the event of the consultation encouraging the iatrogenic access to patients as in our case.

The drug which shares indications, and by which should be replaced in most of the guide lined uses in our service is the morphine. It is a safer drug and, and despite the well-known secondary effects, these can be treated with naloxone (0.5-4 mg/kg per hour) or nalmefene (0.5 g/kg every 6 hours if necessary by means of the intravenous administrated or subcutaneous slow pump).

Studies have brought to light that if determining the probability of dangerous side-effects derivated to the meperidine, they are directly related with the length of the treatment and the consumed amount. Having analyzed the profile of this drug, the side-effects and the ease to produce addiction together with its limited analgesic effect in long term, meperidine has become into an archaic and in disuse. Essentially to quote Dr. David J. Daniels, Demerol is an old heavy dinosaur which must be taken out of use in order to make the efficient pain control a reality.

References

1. Jiang Z (1992) Iatrogenic addiction of pethidine: clinical feature and experience of detoxification. *Zhonghua Shen Jing Jing Shen Ke Za Zhi* 25: 85-87.
2. Latta KS, Ginsberg B, Barkin RL (2002) Meperidine: A critical review. *American Journal of Therapeutics* 9: 53-68.
3. Liu JG, Anand KJ (2001) Protein kinases modulate the cellular adaptations associated with opioid tolerance and dependence. *Brain Res Brain Res Rev* 38: 1-19.
4. Weissman DE, Haddox JD (1989) Opioid pseudoaddiction--an iatrogenic syndrome. *Pain* 36: 363-366.
5. Clubb B, Loveday W, Ballantyne S (2013) Meperidine: a continuing problem. *Subst Abuse* 7: 127-129.
6. Eisendrath SJ, Goldman B, Douglas J (1987) Meperidine-induced delirium. *Am J Psychiatry* 144: 1062-1065.
7. Gaensler EA, McGowan JM, Henderson FF (1947) A comparative study of the action of Demerol and opium alkaloids in relation to biliary spasm. *Surgery* 22: 211-220.
8. Murphree HB (1962) Clinical pharmacology of potent analgesics. *Clin Pharmacol Ther* 3: 473-450.
9. Mather LE, Meffin PJ (1978) Clinical pharmacokinetics of pethidine. *Clin Pharmacokinet* 3: 352-368.