

## EFFICACY OF METHADONE IN DRUG USE DISORDER IN CHRONIC NON-CANCER PAIN

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**Introduction:** Chronic pain is considered one of the most disabling and costly diseases in North America, Europe and Australia. Chronic pain of moderate to severe intensity occurs in 19% of adult Europeans, seriously affecting their daily activities, social and working lives. Chronic pain is a major health care problem in Europe, most of patients are not receiving pain specialist treatment. Italy ranks third in Europe in terms of prevalence of chronic pain; with 26% of the population suffering from chronic pain at some point. The use of opioids in pain management associated with advanced neoplastic disease is widely shared and accepted internationally. However, treatment of chronic non-cancer pain (CNCP) with opioids remains controversial. When the prescription of opioid drugs is aimed at the treatment of CNCP there is evidence of lack of efficacy and complications. The most significant consequences of long-term opioid therapy include tolerance, physical and psychological dependence, abuse and deviation. The aim of this study was to evaluate the safety and efficacy of a long half-life opioid (methadone) in patients with CNCP and opioid use disorder or other symptomatic drugs abuse during a 12-month follow-up.

**Methods:** Patients were retrospectively selected from the database of the Archimed<sup>R</sup> electronic medical record in the Medical-Toxicology Unit of the Careggi University Hospital in Florence. The selection was based on the diagnosis of analgesics abuse in the period from 2012 to 2017. Starting from the first visit other 6 clinical evaluations were analyzed: at baseline (T0), at 1 month (T1), at 3 months (T2), at 6 months (T3), at 9 months (T4), at 12 months (T5). VAS reduction was the primary end-point while reduction of pills per month and the monthly money expenses were the secondary endpoints. The opioid switch was based on Micromedex<sup>R</sup> equianalgesia tables.

**Results:** Our sample included 60 patients: 17 males (28%) and 43 females (72%), with an average age of 48 years (average  $\pm$  SD:  $48 \pm 15$ ). Because of these diagnoses, 37% of patients (n = 22) were unemployed. Psychiatric comorbidity was present in 44 patients (73%) and a third of the sample (28.5%) showed a behavioral pattern of addiction. The 73% (n=44) of patients had an opioid use disorder, 15 took high amounts of AINS daily (25%); paracetamol (20%) or triptans (12%). The most represented form of pain was chronic migraine and cephalalgia. The patients were treated with medium-low dose of methadone hydrochloride (MT). The mean initial daily dose of MT was  $22 \pm 2$  mg. More than a half of the patients (36%) found therapeutic efficacy and completed 12 months of observation with no serious adverse effects reported (responders) with significant VAS reduction. On the contrary for 13 patients (22%) the treatment was not effective in pain control and MT was interrupted by tapering (non responders). Adverse drug reactions (ADRs) were registered for 11 patients, in most cases constipation, nausea or vomiting. Only in one case the interruption was due to long QT interval (QTc = 471 ms). There were also 13 (22%) drop-outs with no ADRs, 5 of which for distrust or stigma for MT. Three patients died during therapy due to causes not related to methadone treatment. Both the Pills per month and money per months were significantly reduced in the responders group.

**Discussion and conclusion:** MT, in the form of a racemate, has proved useful and safe in the clinical management of opioid use disorder ameliorating pain control, reducing VAS, pills per months and prescription drug expenses. Unfortunately MT is a strongly stigmatized drug but difficult to replace due to its peculiar characteristics. MT treatment can provide a chance for patients otherwise lacking effective alternatives. Even in those who do not report benefit from the point of view of analgesia or manifest adverse reactions, MT was able to reduce the abuse of symptomatic drugs and the cost of therapy.