

# Review of: "Methadone: from Chronic Non-Oncological pain and primary Management Of Opioid Hyperalgesia to Disassuefaction Of Painkillers Abuse"

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It has been indicated that the therapeutic potential of methadone was evaluated in the treatments of "Chronic Non-Oncological Pain", "Primary Management of Opioid Hyperalgesia" and "Prevention of Painkiller Abuse".

- No comment on opioid hyperalgesia in the conclusion which is part of abstract, why? The abstract of this manuscript does not match the article title. In addition, I suggest that it should avoid from the exaggerated phrases.
- Is this a systematic review? If so, how many articles were scanned? Why the inclusion and exclusion criteria were not specified. If this is not a systematic review, why were indicated the searched databases?
- Detailed explains can be informative, but not good for integrity. Every sentence and section used must have a purpose. For example; the chemical formulation of methadon are well described in detail, but why? The relationship is absent.
- One sentence that caught my attention is that; *"In particular compounds such as codeine, tramadol and oxycodone are, in Italy, the most prescribed for various types of pain (in the USA other compounds such as hydromorphone, hydrocodone etc ... have far exceeded hospital accesses for overdose compared to the same heroin)"* Such a generalization cannot be made. This is impossible. Almost all of the guidelines related pain management are recommend a step therapy algorithm in the pain treatment: 1) Non-steroidal anti-inflammatory drugs (NSAIDs) 2) Combination of a weak opioid such as codeine, and paracetamol or some of other NSAIDs 3) Opioids. It is absolutely impossible and unacceptable for opioids to be the most preferred analgesic drugs according to this algorithm. Do the authors mean to state that codeine, tramadol, and oxycodone are the most commonly used OPIOD drugs? If so, they should support this by using the relevant epidemiological studies as references.
- It is should produced an abbreviation list or abbreviations are should reviewed again.
- Another expression that caught my attention is that location of this sentence: *"MTD has proved to be a relatively safe and manageable drug in clinical practice.[15]"*. When explaining risks of any drugs, you can't talk about how its safe, or not this way. A logical flow must be followed. There are many similar errors.
- Are the authors suggesting that methadone should be the primary narcotic analgesic? If so or not, it should holistically discuss its advantages and disadvantages over other opioids.

Finally, I'm sad, however I have to say followed that:

- The writing language of the article is weak and not scientific. It needs to be improved. I recommend that long sentences which cause a lot of grammatical errors should be avoided. If necessary, professional support should be sought.
- There is no unity of flow both inside paragraphs themselves and in the whole manuscript. The informations are

disheveled, it is impossible to understand the intended message. The article needs to be handled again as a whole and it should reviewed.