

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

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Potential competing interests: The author(s) declared that no potential competing interests exist.

Dear authors,

thank you for the careful written article about methadone characteristics. however, i don't think it fulfills the criteria of a systematic review.

Please see below my comments for the individual sections

Introduction:

- Focus on chronic pain and importance on treatment
- Little information about painkiller abuse/methadone itself

Methods:

- Not clear, which articles has been reviewed
 - how where included articles assessed/reviewed , what for?
- What type of review is this?

Results? - section missing. how many papers included (original articles, reviews? etc)

- i think 35 papers as reference for a review, which is not time-limited and include lots of keywords seems a very small number. how was further selected

Discussion:

- Very widespread and tries to cover lots of topics
 - 1. Characteristics (chemical properties)
 - 2. Painkiller abuse
 - 3. Pharmacokinetics
 - 4. Tolerance of opioid
- more opinion distribution rather than discussing of the relevant papers
- Biased listening of facts rather than discussion of results from various studies
- Start is a summary about its characteristics, which would be easier to implement in introduction

- Please check Spelling errors
- Effects of d-methadone – according to literature effect is unclear. It is also considered antidepressant, more effect on ECG trace.
- Please reference for antitussive effects and list other papers looking at properties of both enantiomers
- I think the role of methadone as alternative in treatment of opioid induced hyperalgesia is not clearly distinguished from abuse – similarly, is this situation (type 2 patients) actually really considered as abuse?
- the topic “primary management of opioid hyperalgesia” is not really discussed (evidence, original papers), also underlying background informations are missing
- Image 2b: what does the abbreviations means? source of image or data?

conclusion:

makes a more straight forward attempt, however, discussion of literature in general is not sufficient

i would recommend this as a letter to the editor (or whatever is equivalent in qeios) to highlight its importance, but it does not fulfill the criteria for a thorough systematic review