INESSS
LE SAVOIR PREND FORME

MAY 2021

Efficacy and safety of buprenorphine and methadone for the treatment of opioid use disorder

English summary

Une production de l'Institut national d'excellence en santé et en services sociaux (INESSS)

Québec

SUMMARY

Efficacy and safety of buprenorphine and methadone for the treatment of opioid use disorder

Introduction

Opioid use disorder (OUD) is associated with high rates of mortality and morbidity. Methadone and the sublingual formulation of buprenorphine-naloxone are the two main opioid agonists indicated by Health Canada for the treatment of OUD. Although methadone has been used for this indication for over 40 years, its use raises certain questions regarding quality of life and safety for those being treated, particularly because of its high number of interactions with other medications and possible QT interval prolongation. Buprenorphine, on the other hand, is a partial opioid agonist that produces a plateau effect which appears to decrease the risk of overdose and adverse effects (e.g., cardiac arrhythmia), as well as withdrawal symptoms when the treatment is discontinued.

A systematic review of the available scientific data was therefore conducted in order to take a position regarding the preferred pharmacological treatment options for opioid use disorder while developing an optimal use guide on oral opioid agonists for the treatment of OUD.

Methodology

Systematic literature review

To assess the efficacy and safety of buprenorphine compared to methadone, a systematic search was conducted within several bibliographic databases from their date of inception to February 2020 to identify all relevant published primary research studies and systematic reviews, with or without meta-analyses.

Documents were selected according to predefined inclusion and exclusion criteria. The quality of the selected documents was assessed using appropriate tools. These steps were performed independently by two reviewers. Data were then extracted by one reviewer and validated by the other. The results were presented in tables and summarized in the form of an analytical narrative synthesis.

Process for assessing quality of the scientific evidence

The main efficacy and safety results reported in the retained studies were expressed as brief statements of scientific evidence. An overall level of scientific evidence was assigned to each statement of evidence according to a four-level scale (high, moderate, low, insufficient).

Results

The systematic literature review conducted by INESSS looked at retention rates, the duration of therapeutic adherence, quality of life, drug use rates, mortality rates, and adverse effects of buprenorphine compared to methadone.

The efficacy data extracted from the retained studies showed broadly similar results for the two treatments, at a moderate to high level of evidence, regarding retention rate, duration of therapeutic compliance and quality of life, when comparable doses were used. However, duration of therapeutic adherence appeared to be shorter with buprenorphine, based on a high level of evidence, when daily doses of 8 mg or less are used. Otherwise, rates of opioid use and other drug use were similar or lower overall in individuals treated with buprenorphine compared to those treated with methadone, at a moderate to high level of evidence.

The findings regarding retention rates, quality of life, and rates of opioid and other drug use appeared to also apply to pregnant women and individuals with co-existing chronic pain. Similarly, the findings concerning duration of therapeutic compliance and safety appeared to apply to pregnant women. However, the number of studies involving these populations was much smaller than that for the general population.

Additionally, the all-cause mortality rate was found to be similar for the two treatments, based on a moderate level of evidence, during both the entire treatment period and the maintenance period. However, during the treatment induction period, the all-cause mortality rate was lower for those treated with buprenorphine compared to those treated with methadone, at a high level of evidence. In addition, the opioid-related poisoning mortality rate was lower with buprenorphine than with methadone, regardless of the treatment period, based on a moderate to high level of evidence.

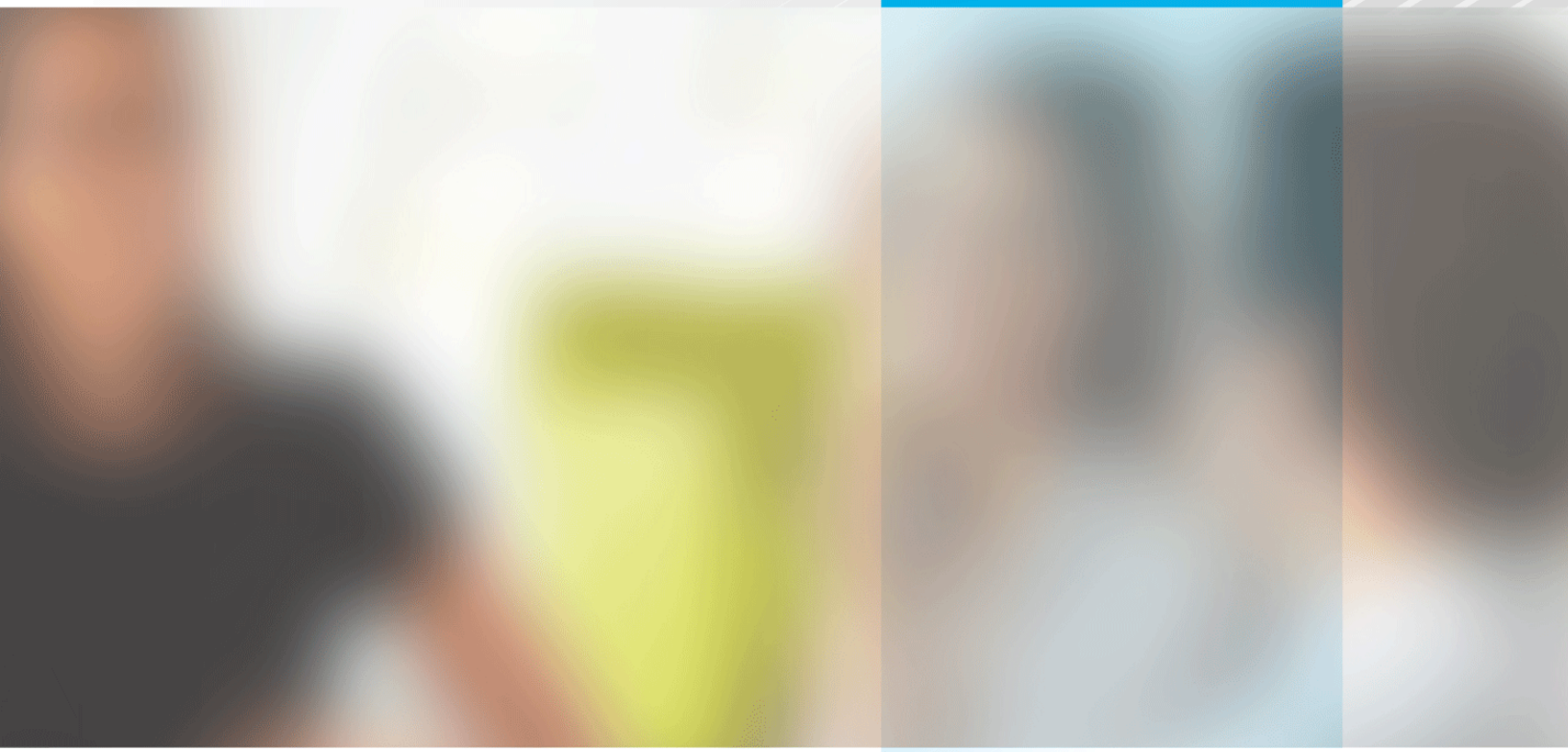
With respect to safety, the rates of adverse effects observed in the retained studies were similar for buprenorphine and methadone, regardless of the study dose and in both adults and pregnant women, based on a high level of evidence. However, a lower occurrence of fatigue, stomach cramps, loss of appetite, migraine, constipation and sedation was observed with buprenorphine than with methadone. A lower frequency of minor problems and a higher gestational age at birth was also observed with buprenorphine compared to methadone. As well, the rate of newborns requiring treatment for neonatal abstinence syndrome (NAS) was similar or lower in those born to mothers who were treated with buprenorphine rather than methadone, at a moderate level of evidence. The length of hospitalization for newborns with NAS was shorter for those whose mothers were treated with buprenorphine versus methadone, based on a high level of evidence.

In the specific case of the buprenorphine-naloxone formulation, the rate of newborns requiring treatment for SAN was lower and the length of hospitalization was shorter or similar for those born to mothers who were treated with buprenorphine-naloxone compared to mothers treated with methadone, based on a low level of evidence. However, rates of adverse effects in terms of preterm deliveries and the physical

characteristics of the infant (weight, height and head circumference) were similar in the two groups, based on a low level of evidence.

Conclusions

The scientific evidence examined in this systematic review was supplemented with contextual information and experiential knowledge in order to develop the recommendations set out in the OUG on oral opioid agonists for the treatment of opioid use disorder. This process is presented in detail in the companion report supporting the OUG on this topic [(INESSS), 2021]. The present systematic review also revealed the need for adequate clinical studies on a larger number of individuals with concurrent chronic pain, for greater homogeneity in the doses used, and for longer follow-up to better define the situations in which buprenorphine or methadone can provide therapeutic benefit.



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