Efficacy and safety of pharmacological treatments for alcohol withdrawal and relapse prevention
Systematic review report
English summary

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

Efficacy and safety of pharmacological treatments for alcohol withdrawal and relapse prevention
Systematic review report

Introduction

Alcohol abuse is associated with considerable morbidity. Additionally, alcohol withdrawal after prolonged and heavy consumption can result in symptoms of varying severity that can cause suffering or impaired functioning and that can progress to major complications, such as confusion, seizures or delirium tremens. Although benzodiazepines are generally considered the first-line treatment for alcohol withdrawal syndrome, their use carries certain risks, including an increase in the effects of alcohol, significant adverse effects, and the potential for dependence and misuse. Yet, people with alcohol use disorder (AUD) may benefit from pharmacotherapy to help them reduce their alcohol consumption or prevent a return to alcohol abuse. Only naltrexone and acamprosate are approved by Health Canada for relapse prevention or maintenance of abstinence in individuals with AUD. These two drugs are often out of stock, which can compromise their access to pharmacotherapy.

Given that anticonvulsants are sometimes used clinically for either of these indications, a systematic review of the available scientific data on these drugs was carried out to shed light on the best pharmacological treatment options for the purpose of developing the optimal use guide (OUG) and Québec national medical protocols on treatments for alcohol withdrawal and relapse prevention.

Methodology

Systematic literature reviews

To assess the efficacy and safety of anticonvulsants for alcohol withdrawal and of anticonvulsants and baclofen for relapse prevention, systematic reviews were performed across several bibliographic databases, which were searched from the period from the date of their inception to May 2020, with the aim of identifying all the primary studies and systematic reviews, with or without a meta-analysis, published on the subject.

Items were selected according to predefined inclusion and exclusion criteria, and the quality of these items was assessed using the appropriate tools. These steps were carried out independently by two reviewers. The 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 the quality of the scientific evidence

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

Results

Alcohol withdrawal

For the treatment of alcohol withdrawal, the systematic literature reviews focused on the efficacy and safety of anticonvulsants compared to benzodiazepines.

First, data extracted from the selected studies comparing anticonvulsants and benzodiazepines showed similar efficacy and safety for:

- Gabapentin, at a daily dose of at least 900 mg, for the treatment of mild to moderate alcohol withdrawal, based on a level of evidence considered low to moderate;
- Valproic acid, for the treatment of moderate alcohol withdrawal, based on an overall level of evidence considered low;
- Carbamazepine, for the treatment of moderate to severe alcohol withdrawal, based on an overall level of evidence considered low to moderate.

As well, gabapentin appears to cause less drowsiness than benzodiazepines. As for lamotrigine and topiramate, they have similar efficacy and greater safety compared to benzodiazepines in the treatment of moderate to severe alcohol withdrawal, based on an overall level of evidence considered low. Pregabalin appears to be more effective than benzodiazepines in terms of the proportion of participants who do not use alcohol and in reducing psychiatric symptoms, and is similar to benzodiazepines in terms of safety in the treatment of moderate to severe alcohol withdrawal, based on an overall level of evidence considered low. However, the scientific data do not permit any conclusions to be drawn regarding the efficacy of pregabalin compared to benzodiazepines in lowering the CIWA-Ar score. Lastly, phenobarbital and benzodiazepines have similar efficacy in the treatment of mild to severe alcohol withdrawal, based on an overall level of evidence considered moderate. However, the scientific evidence does not permit any conclusions to be drawn regarding the safety of phenobarbital compared to benzodiazepines.

Relapse prevention

With respect to treatment for relapse prevention, the systematic literature reviews focused on the efficacy and safety of anticonvulsants or baclofen compared to naltrexone, acamprosate or placebo.
First, topiramate is generally more effective than placebo, naltrexone and acamprosate, based on an overall level of evidence considered low to moderate. Furthermore, topiramate does not appear to cause any serious adverse effects up to daily doses of 300 mg, based on a high level of evidence. As well, topiramate has similar safety to placebo or naltrexone when initiated over a longer period of time but appears to have greater safety than acamprosate, based on an overall level of evidence considered low. Second, gabapentin at a daily dose of at least 1200 mg has greater efficacy and similar safety compared to placebo, based on an overall level of evidence considered low to moderate. However, drowsiness appeared to be more common with gabapentin. As for baclofen, it has similar efficacy and safety compared to placebo, based on an overall level of evidence considered low to moderate. However, when used at a daily dose of at least 180 mg, baclofen has greater efficacy but is less safe than placebo, based on an overall level of evidence considered low to moderate. Furthermore, baclofen has greater efficacy and similar safety compared to acamprosate, based on an overall level of evidence considered low. Lastly, carbamazepine, pregabalin and valproic acid have generally similar efficacy and safety compared to placebo, based on an overall level of evidence considered low. However, drowsiness appeared to be more common with valproic acid than with naltrexone.

Conclusion

The results presented in this systematic review (SR) report provided the scientific information needed to develop the recommendations in the OUG and the Québec national medical protocols on pharmacological treatments for alcohol withdrawal and relapse prevention. This systematic review has also highlighted the need for clinical studies of good methodological quality that would be more homogeneous in terms of the participants included, the evaluation instruments, the drug doses studied and the outcome parameters chosen in order to better assess the efficacy and safety of the various pharmacotherapeutic options available, particularly for certain treatments for which very little scientific data was found.