World Hepatitis Day
28th July 2023

Background and keys informations

In 1967, Dr. Baruch Blumberg (1925-2011) discovered the hepatitis B virus. Two years later, he also developed the first vaccine against hepatitis B. Dr. Blumberg was born on July 28, which is why World Hepatitis Day is celebrated today. Infection with the hepatitis B virus can be prevented by vaccination. It should also be added that doctors can now effectively treat hepatitis C, caused by the hepatitis C virus, with antiviral drugs.

Hepatitis causes damage to the normal structure of the liver, preventing it from functioning properly. The theme of this year's edition, One Life, One Liver, aims to focus on the link between viral hepatitis and liver inflammation - i.e. liver damage and injury - as well as on the broader issues of liver health and primary healthcare. Hepatitis B is generally transmitted from mother to child during delivery or at birth. It can also be transmitted through contact with blood or other biological fluids during sexual relations with an infected partner, high-risk injections, or exposure to sharp instruments.

Hepatitis C is transmitted by contact with the blood of an infected person: unscreened blood transfusions, sharing needles or risky sexual practices involving direct exposure to blood. More than 91 million Africans are living with hepatitis. In 2019, an estimated 1.2 million new hepatitis infections were recorded in the African Region, along with 125,000 hepatitis-related deaths. These deaths occur mainly among young, productive segments of the population. The World Health Organization's (WHO) Global Hepatitis Strategy - endorsed by all WHO Member States - and the Framework for an Integrated Multisectoral Response to Tuberculosis, HIV, Sexually Transmitted Infections and Hepatitis in the WHO African Region, aim to reduce new hepatitis virus infections by 90% and hepatitis-related deaths by 65% by 2030.

The World Health Organization's (WHO) Global Hepatitis Strategy - endorsed by all WHO Member States - and the Framework for an Integrated Multisectoral Response to Tuberculosis, HIV, Sexually Transmitted Infections and Hepatitis in the WHO African Region, aim to reduce new hepatitis virus infections by 90% and hepatitis-related deaths by 65% by 2030. WHO supports regional and national efforts to eliminate viral hepatitis by 2030. Indeed, the Organization is providing clear guidance, including for decentralized and simplified prevention, screening and treatment of viral hepatitis, with an emphasis on a person-centered approach. This includes eliminating hepatitis B by administering a dose of vaccine at birth (on the day of birth or the day after).

Much remains to be done to reduce the number of deaths and infections linked to this disease. Despite the availability of effective diagnostic tools and treatments, over 90% of people living with hepatitis in Africa do not receive the care they need, and less than 10% of the population has access to screening and treatment services. This encourages the progressive advance of liver disease, imposes a catastrophic financial burden and leads to repercussions such as emotional distress and stigmatization. Screening and treatment remain the most neglected aspects of the proposed public health response.

The highest prevalence of hepatitis B infection in children under the age of five is found in countries where hepatitis B vaccination is not carried out at birth. Vaccination is therefore an important component in the fight against hepatitis. I am pleased to note that all 47 Member States of the African Region have included hepatitis B vaccine in routine immunization. However, routine hepatitis B vaccination coverage for children in the Region stands at 72%, well below the global target of 90%. By 2022, 16 countries in the region have begun administering a dose of hepatitis vaccine to all newborns, compared with 11 countries in 2021 (WHO, 2023).

As part of this celebration, the Center for the Development of Best Practice in Health, propose these summaries of Cochrane systematic reviews aiming to inform the patients, medical staff and others stakeholders on the prevention and management of hepatitis.

JOURNEE MONDIALE DE LUTTE CONTRE LES HEPATITES

Contexte et informations clés

En 1967, le Dr Baruch Blumberg (1925-2011) a découvert le virus de l'hépatite B. Deux ans plus tard, il a également mis au point le premier vaccin contre l'hépatite B. Le Dr Blumberg est né le 28 juillet et c'est la raison pour laquelle la Journée mondiale contre l'hépatite est célébrée aujourd'hui.

L'infection par le virus de l'hépatite B peut être évitée par la vaccination. Aussi convient-il d'ajouter que désormais, les médecins peuvent traiter efficacement l'hépatite C, causée par le virus de l'hépatite C, au moyen de médicaments antiviraux.

L'hépatite entraîne une dégradation de la structure normale du foie, empêchant ainsi le bon fonctionnement de cet organe. Le thème retenu pour l'édition de cette année, à savoir Une vie, un foie, vise à mettre l'accent sur le lien entre l'hépatite virale et l'inflammation du foie – c'est-à-dire les lésions et dommages au foie, – ainsi que sur les questions plus générales de la santé du foie et des soins de santé primaires.

L'hépatite B se transmet généralement de la mère à l'enfant pendant l'accouchement ou à la naissance. Elle peut aussi se transmettre par contact avec du sang ou d'autres liquides biologiques lors de rapports sexuels avec un partenaire infecté, d'injections à risque, ou en cas d'exposition à des instruments tranchants ou piquants.

L'hépatite C se transmet quant à elle par contact avec le sang d'une personne infectée : transfusions sanguines sans dépistage, partage d'aiguilles ou pratiques sexuelles à risque provoquant une exposition directe au sang.

Plus de 91 millions d'Africains vivent avec l'hépatite. En 2019, selon les estimations, 1,2 million de nouvelles infections par le virus de l'hépatite ont été enregistrées dans la Région africaine, de même que 125 000 décès liés à cette maladie. Des décès qui surviennent principalement parmi les franges de population comprenant des personnes jeunes et productives.

La Stratégie mondiale proposée par l'Organisation mondiale de la Santé (OMS) contre l'hépatite, – approuvée par l'ensemble des États Membres de l'OMS – , tout comme le Cadre pour une riposte multisectorielle intégrée à la tuberculose, à l'infection à VIH, aux infections sexuellement transmissibles et à l'hépatite

dans la Région africaine de l'OMS, vise à réduire de 90 % les nouvelles infections par le virus de l'hépatite et de 65 % les décès dus à cette maladie d'ici à 2030.
L'OMS soutient les efforts déployés aux niveaux régional et national en vue d'éliminer l'hépatite virale à l'horizon 2030. En effet, l'Organisation fournit des orientations claires, notamment pour une prévention, un dépistage et un traitement décentralisés et simplifiés de l'hépatite virale, en mettant l'accent sur une approche centrée sur la personne. Cela inclut l'élimination de l'hépatite B par l'administration d'une dose de vaccin à la naissance (dès le jour de la naissance ou le lendemain).
Il reste encore beaucoup à accomplir pour réduire le nombre de décès et le nombre d'infections liées à cette maladie. Malgré la disponibilité d'outils de diagnostic et de traitements efficaces, plus de 90 % des personnes vivant avec l'hépatite en Afrique ne reçoivent pas les soins dont elles ont besoin et, moins de 10 % de la population jouit d'un accès aux services de dépistage et de traitement. Cela favorise l'avancée progressive des maladies hépatiques, occasionne une charge financière catastrophique et induit des répercussions telles que la détresse émotionnelle et la stigmatisation. Le dépistage et le traitement restent les aspects les plus négligés de la riposte proposée au titre de l'approche de santé publique.
La prévalence la plus élevée de l'infection par le virus de l'hépatite B chez les enfants âgés de moins de cinq ans est constatée dans les pays où la vaccination anti-hépatite B n'est pas réalisée à la naissance. La vaccination est donc une composante importante de la lutte contre l'hépatite. Je suis heureuse de constater que tous les 47 États Membres de la Région africaine ont inclus le vaccin contre l'hépatite B dans la vaccination systématique. Cependant, la couverture de la vaccination systématique des enfants contre l'hépatite B dans la Région se situe à 72 %, bien en deçà de la cible mondiale fixée à 90 %. En 2022, 16 pays de la Région ont procédé, dès la naissance, à l'administration d'une dose du vaccin anti-hépatique à tous les nouveau-nés, contre 11 pays en 2021 (OMS, 2023).

Dans le cadre de la célébration de la journée mondiale de lutte contre les Hépatites, le Centre pour le développement des Bonnes pratiques en santé, propose ce recueil de résumés de revues systématiques Cochrane visant à informer les patients, le personnel médical et les autres parties prenantes sur la prévention et la prise en charge des hépatites.

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1- Antivirals for prevention of hepatitis B virus mother-to-child transmission in human immunodeficiency virus positive pregnant women co-infected with hepatitis B virus

Review question

Can antenatal (administered during pregnancy) antiviral combination drugs prevent transfer of hepatitis B virus from mother to baby in pregnant women suffering from both human immunodeficiency virus (HIV) and hepatitis B virus (HBV)?

Key messages

The evidence from five small randomised clinical trials showed neither beneficial nor harmful effects of tenofovir-containing antiviral combination drugs compared with zidovudine alone or non-tenofovir-containing antiviral drugs, in pregnant women suffering from both HIV and HBV, measured by infant death from any cause, or serious adverse events in infants and mothers.

Only one trial reported on infant death from any cause or serious adverse events in infants while only two trials reported on serious adverse events in mothers.

Whilst this trial indicated that a tenofovir-based antiviral combination regimen could increase the number of infants with serious adverse events, this result is very uncertain due to the lack of studies (i.e. only one was found) and the low number of participants.

What is HBV-HIV co-infection in pregnancy?

The HBV-HIV co-infection in pregnancy is the occurrence of the two infections in one pregnant individual. When the two infections co-exist in an individual, HIV actively encourages the worsening of hepatitis B disease progression. When a pregnant woman is living with both HBV and HIV, treatment of HBV alone, without treating the HIV she also suffers from, may lead to the emergence of HIV types that are resistant to anti-HIV drugs.

How is HBV-HIV co-infection in pregnancy treated?

HBV-HIV co-infection in pregnancy can be treated with tenofovir-based antiviral combination regimens (drugs). They could be in the form of tenofovir alone or in combination with lamivudine, or emtricitabine, or zidovudine, or any other antiviral drugs.

What did we want to find out?

We wanted to find out whether antenatal use of tenofovir-containing antiviral combination drugs (drugs administered during pregnancy) was better than placebo, or tenofovir alone, or any non-tenofovir-containing antiviral drugs (either alone or in combination with at least two), for improving all causes of death for both baby and mother, transfer of HBV infection from mother to baby, mothers with detectable HBV DNA (hepatitis B hereditary material) before delivery, or maternal hepatitis B

seroconversion (recovery from hepatitis B) before delivery in pregnant women living with both HIV and HBV.

We also wanted to find out if antenatal use of tenofovir-containing antiviral combination drugs (drugs administered during pregnancy) compared with placebo, or tenofovir alone, or any non-tenofovir-containing antiviral drugs (either alone or in combination with at least two), was associated with any unwanted effects in the baby and mother.

What did we do?

We searched for randomised clinical trials (studies in which participants are allocated to groups by a play of chance) that assessed the benefits and harms of antenatal use of tenofovir-containing antiviral combination drugs (drugs administered during pregnancy), compared with placebo, or tenofovir alone, or any non-tenofovir-containing antiviral drugs (either alone or in combination), for pregnant women living with both HIV and HBV infection. We compared and summarised the results of the studies and rated our confidence in the evidence, based on factors such as study methods and sizes.

What did we find?

We found five randomised trials that included 533 pregnant women suffering from both HIV and HBV who were followed up throughout pregnancy and delivery with their infants being followed up to two years after birth. All the results were inconclusive between groups. The evidence from five small randomised clinical trial showed neither beneficial nor harmful effects of tenofovir-containing antiviral combination drugs compared with zidovudine alone, or non-tenofovir-containing antiviral drugs, in pregnant women suffering from both HIV and HBV, measured by infant death from any cause, or serious adverse events in infants and mothers. Only one trial reported on infant death from any cause or serious adverse events in infants, while only two trials reported on serious adverse events in mothers. Whilst this trial indicated that a tenofovir-based antiviral combination regimen could increase the number of infants with serious adverse events, this result is very uncertain due to the lack of studies (i.e. only one was found) and the low number of participants. We did not find data on the other outcomes of interest. None of the studies used placebo or tenofovir alone. All the trials received support from industry.

What are the limitations of the evidence?

We are not confident in the evidence because not all the studies provided data about everything that we were interested in. It was not clear whether people in the studies were aware of which treatment they were receiving. Also, there were not enough studies to be certain about the results of our outcomes.

How up-to-date is this evidence?

The evidence is up-to-date to 30 January 2023.

Authors' conclusions

Implications for practice

Based on the results of key clinical outcomes in this systematic review, we can neither demonstrate nor disprove any benefit of effects of tenofovir-containing antiviral combination drugs versus any non-tenofovir-containing antiviral drugs for the prevention of mother-to-child transmission of HBV in HIV-positive pregnant women co-infected with HBV. So, the decision to use an antiviral drug or its combination, and the choice of type could be based on the physician's and patient's values and preferences, or their availability.

Implications for research

We need large, high-quality randomised clinical trials to assess the role of tenofovir-containing antiviral combination drug regimens for the prevention of mother-to-child transmission of HBV in HIV-positive pregnant women co-infected with HBV. Such randomised clinical trials should be designed according to the SPIRIT guidelines (Standard Protocol Items: Recommendations for Interventional Trials; www.spiritstatement.org) and reported according to the CONSORT guidelines (www.consort-statement.org; Butcher 2022). Given the burden of co-infection with HIV and HBV in resource-limited contexts, we recommend more pragmatic trials that will consider cost-effectiveness as an outcome.

Citation : Ugwu EO, Eleje GU, Ugwu AO, Nwagha UI, Ikechebelu JI, Umeh UA, Okafor HU. Antivirals for prevention of hepatitis B virus mother-to-child transmission in human immunodeficiency virus positive pregnant women co-infected with hepatitis B virus. Cochrane Database of Systematic Reviews 2023, Issue 6. Art. No.: CD013653. DOI: 10.1002/14651858.CD013653.pub2. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013653.pub2/full/fr#CD013653-abs-0002

2- Rifaximin for prevention and treatment of hepatic encephalopathy in people with cirrhosis

Key messages

The prevention and treatment of hepatic encephalopathy, in people with cirrhosis, largely depends on use of the compound lactulose. Rifaximin is not used to treat hepatic encephalopathy, at present, but it is used as an add-on to lactulose to help prevent hepatic encephalopathy in people whose response to lactulose is inadequate.

We found that combining rifaximin with lactulose improved hepatic encephalopathy, reduced the risk of dying, and reduced the risk of developing side effects in addition to preventing future relapses.

Its wider use in the management of people with hepatic encephalopathy needs to be considered.

What are cirrhosis and hepatic encephalopathy?

Cirrhosis is a long-term condition in which scar tissue (fibrosis) replaces normal liver tissue, often as a result of excess alcohol, being overweight, or having chronic hepatitis B/C infection. People with cirrhosis commonly develop a condition called hepatic encephalopathy which affects their mental function and their neurological function. This condition can have a negative effect on their survival. The exact reason why people with cirrhosis develop hepatic encephalopathy is unknown, but the toxin ammonia, which is produced mainly in the gut, is thought to play an important role. The severity of the symptoms of hepatic encephalopathy ranges from minor difficulties in mental function to obvious changes in movement, mental status, and consciousness. The minor changes in concentration, behaviour, and everyday function are classed as minimal hepatic encephalopathy. The more obvious abnormalities and changes in consciousness are classed as overt hepatic encephalopathy. The overt symptoms may occur in episodes or may be present at all times.

How is hepatic encephalopathy treated?

The non-absorbable disaccharides (sugars), lactulose and lactitol, are the most commonly used treatment for hepatic encephalopathy. They reduce ammonia levels in the blood through multiple actions, mainly in the gut. Rifaximin is an antibiotic that is not absorbed into the blood stream but works solely in the gut, where it reduces the production of ammonia by the gut bacteria and ammonia absorption into the blood system. This effect may benefit people with hepatic encephalopathy.

What did we want to find out?

We wanted to find out if rifaximin could be used to prevent and treat hepatic encephalopathy in people with cirrhosis; whether it does this better than no drug treatment, a dummy pill (placebo), or non-absorbable disaccharides; whether there may be additional benefit if rifaximin is used together with a non-absorbable disaccharide; and whether there were any unwanted side effects.

What did we do?

We searched for studies that looked at rifaximin compared with no treatment, placebo, or non-absorbable disaccharides in people with cirrhosis with, or at risk for developing, hepatic encephalopathy. We also searched for studies that used rifaximin plus non-absorbable disaccharides compared with non-absorbable disaccharides alone.

We compared and summarised the results of the studies and rated our confidence in the evidence, based on factors such as study methods and sizes.

What did we find?

We identified 41 clinical studies involving 4545 people, who were randomly allocated to treatment groups. All participants had cirrhosis mainly due to excessive alcohol intake or chronic viral hepatitis. Participants were classed as having acute (13 studies), chronic (7 studies), or minimal (8 studies) hepatic encephalopathy, or were considered to be at risk for its development (13 studies). The studies compared rifaximin with a placebo (12 studies), no intervention (1 study), or lactulose/lactitol (14 studies). In 18 studies, rifaximin was given together with lactulose/lactitol and the results compared to the effect of giving lactulose/lactitol alone.

The analyses found that giving rifaximin alone may help improve health-related quality of life and the performance of tests used to assess mental function in people with minimal hepatic encephalopathy. However, lactulose is probably as effective and is considerably cheaper. There were no differences in the benefits and side effects of rifaximin when directly compared with lactulose/lactitol. However, when rifaximin was given together with lactulose/lactitol, it reduced the risk of death (from 14.8% to 10.1%), reduced the risk of unwanted side effects (from 34.4% to 17.6%), and resulted in improvement in hepatic encephalopathy (from 86.9% to 33.8%) when compared to use of lactulose alone.

What are the limitations of the evidence?

We are uncertain about or have only moderate confidence in our findings, meaning we cannot make more certain conclusions about the effects of rifaximin. This was mainly because people in the studies might have been aware of which treatment they were getting and not all the studies provided data about the outcomes we were interested in. Also, many studies were too small for us to be certain about their results. More high-quality studies are needed.

How up to date is this evidence?

The evidence is up to date to January 2023.

Authors' conclusions

Implications for practice

The evidence provided in this review suggests that rifaximin, particularly when used in combination with a non-absorbable disaccharide, may have a place in the management of people with cirrhosis and hepatic encephalopathy. The certainty of the evidence is generally low, but some implications for practice can be deduced. Minimal hepatic encephalopathy detrimentally affects the performance of complex tasks, compromises personal safety, significantly impairs health-related quality of life, and is a major risk factor for the development of overt hepatic encephalopathy. Treatment with rifaximin confers benefit in minimal hepatic encephalopathy, but its effects are not superior to those of non-absorbable disaccharides, except to lower

blood ammonia. Considering the clinical course of the condition, it is likely that treatment, once instigated, would need to be continued in the long term. Current cost considerations may favour use of a non-absorbable disaccharide for this indication.

Development of an episode of acute hepatic encephalopathy is associated with significant reductions in short- and medium-term survival. Rifaximin and non-absorbable disaccharides may have equivalent effects on mortality and clinical recovery when used for this indication. However, combining the use of rifaximin with a non-absorbable disaccharide may have beneficial effects on both mortality and resolution of the hepatic encephalopathy compared to use of a non-absorbable disaccharide alone, with likely no increase in the risk of adverse events. While the combined use of rifaximin and lactulose is not licensed for this indication, use of the combination could be considered in this situation, particularly if supported by further studies.

The risk of developing further episodes of hepatic encephalopathy following an index event is high. Long-term use of rifaximin and a non-absorbable disaccharide to prevent hepatic encephalopathy may be effective in reducing the risk of recurrence, when compared to a non-absorbable disaccharide alone, but does not influence mortality. Rifaximin is licensed for use, in combination with lactulose, for secondary prevention of hepatic encephalopathy, and our review findings support its use for this indication.

Rifaximin, whether as monotherapy (three trials) or in combination with a non-absorbable disaccharide (one trial), does not appear to benefit chronic hepatic encephalopathy, although the number of included studies in our review was very small, so the evidence is very uncertain. Chronic hepatic encephalopathy is often associated with the presence of large spontaneous portosystemic shunts and consideration should be given to non-invasive obliteration of these, if present. Similarly, consideration should be given to reducing the size of any previously inserted transjugular intrahepatic shunts. The presence of chronic hepatic encephalopathy should be an indication for assessment for liver transplantation, but not for this indication alone.

No implications for practice can be made, based on this review, for the prevention or treatment of hepatic encephalopathy following the insertion of a transjugular intrahepatic portosystemic shunt. Careful selection of candidates for this procedure is the most effective way to reduce the risk of post-shunt hepatic encephalopathy. However, the results of two ongoing studies may help provide guidance.

Likewise, no implications for practice can be made, based on this review, for the treatment of hepatic encephalopathy in acute-on-chronic liver failure.

Implications for research

When selecting trials for inclusion in this review, we identified 13 ongoing trials which might provide data suitable for inclusion in future review updates. Seven of the 13 ongoing trials involve other complications of cirrhosis or are mechanistic, and we are uncertain whether clinically relevant information will be extractable from these when completed. However, the remaining six ongoing trials should provide clinically important data which may allow us to be more certain about the conclusions of our present review. Thus, two trials – one multicentre and one single centre – are comparing rifaximin, with or without adjuvant lactulose, against standard care or placebo for the prevention of encephalopathy following insertion of a transjugular, intrahepatic portosystemic shunt. One trial is investigating rifaximin against placebo for primary prevention of hepatic encephalopathy, while another will investigate rifaximin against placebo for secondary prevention. One trial is investigating rifaximin versus placebo for minimal hepatic encephalopathy, while a further trial is investigating rifaximin versus lactulose for acute hepatic encephalopathy. Although the quality of these trials cannot be assessed until completed and published, the fact that they are funded and are already underway does have implications for future research undertakings.

Fewer than half of the trials included in our review were free of potential bias, and the majority only provided outcome information on hepatic encephalopathy, and less frequently, adverse events and mortality. In addition, a variety of diagnostic and monitoring techniques were used, making comparisons difficult. All future trials should be conducted to rigorous standards; they should use validated diagnostic procedures to characterise the trial populations; they should be designed to avoid bias by use of robust randomisation methods and blinding, and avoid incomplete or selective reporting of data; outcome measures should be predefined and should be robust and clinically relevant; the trials should be adequately powered.

The use of rifaximin to prevent and treat complications of cirrhosis other than hepatic encephalopathy – for example, portal hypertension and spontaneous bacterial peritonitis – is also being explored. These trials could be an important source of additional data on hepatic encephalopathy, and researchers undertaking these trials should be urged to include assessments of mental status and cognitive function. Likewise, researchers undertaking trials of rifaximin in hepatic encephalopathy, especially the longer-term prevention trials, should be encouraged to assess and monitor other potential complications of cirrhosis.

We used the EPICOT format in the definition of implications for research (Brown 2006):

Evidence (what is the current state of the evidence?): this review includes 41 randomised clinical trials; we classed 18 as being at high risk of bias in the overall assessment of mortality and non-mortality and a further 11 as being at high risk for non-mortality outcomes only. We found moderate-certainty evidence for a beneficial effect of rifaximin in minimal hepatic encephalopathy, health-related quality of life, and performance of Number Connection Test A (NCT-A) when compared to placebo. We found very low-certainty evidence for beneficial effects of rifaximin plus a non-absorbable disaccharide on mortality and on hepatic encephalopathy compared to use of a non-absorbable disaccharide alone.

Participants (what is the population of interest?): people with cirrhosis with minimal, acute, and chronic hepatic encephalopathy; people with cirrhosis who are at risk for developing encephalopathy, for example, after a gastrointestinal bleed or insertion of a transjugular intrahepatic portosystemic shunt (primary preventions); people who have experienced one or more previous episodes of encephalopathy (secondary prevention); people with acute-on-chronic liver failure with hepatic encephalopathy.

Interventions (what are the interventions of interest?): rifaximin as monotherapy or combined with a non-absorbable disaccharide.

Comparisons (what are the comparisons of interest?): placebo-controlled trials of rifaximin could be considered in minimal hepatic encephalopathy and for primary prevention; some primary prevention trials have compared rifaximin with placebo and with other active agents such as lactulose and L-ornithine L-aspartate. Non-absorbable disaccharides are the treatment of choice for hepatic encephalopathy and there appears to be additional benefit in combining the use of rifaximin with lactulose; future trials in acute/chronic hepatic encephalopathy and secondary prevention should compare rifaximin plus lactulose against lactulose and a placebo preparation. Trials of new, potentially active drugs should include suitably-blinded comparisons with rifaximin, lactulose, and rifaximin plus lactulose.

Outcomes (what are the outcomes of interest?): information on mortality, hepatic encephalopathy, and adverse events should be collected in all future trials; health-related quality of life is an outcome of interest, except in trials in acute hepatic encephalopathy where data would be difficult to obtain; surrogate markers such as psychometric tests and biomarkers such as blood ammonia, collected at the beginning and the end of treatment periods, are of value, particularly in trials in minimal hepatic encephalopathy.

Citation : Zacharias HD, Kamel F, Tan J, Kimer N, Gluud LL, Morgan MY. Rifaximin for prevention and treatment of hepatic encephalopathy in people with cirrhosis. Cochrane Database of Systematic Reviews 2023, Issue 7. Art. No.: CD011585. DOI: 10.1002/14651858.CD011585.pub2. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD011585.pub2/full/fr#CD011585-abs-0002

3- The combination of transcatheter arterial chemoembolisation (TACE) and thermal ablation versus TACE alone for hepatocellular carcinoma

Background

Hepatocellular carcinoma (a common kind of liver cancer) is the sixth most common cancer in the world. Transcatheter arterial chemoembolisation (TACE) (injecting agents into the feeding vessels of the tumour to reduce the blood supply to the tumour and kill the tumour) is the most common therapy for hepatocellular carcinoma, but the clinical outcome is poor. In recent years, the combination of TACE plus thermal ablation (killing the tumour cell by producing heat or cold) has shown better efficacy than TACE alone. However, evidence to prove the beneficial or harmful effect of the combination of TACE with ablation for people with hepatocellular carcinoma is still lacking.

Aim

We aimed to assess the beneficial and harmful effects of the combination of TACE with thermal ablation versus TACE alone for hepatocellular carcinoma.

Key results

We considered 135 records eligible for full-text screening. We excluded 21 of these records because the interventions used were outside the scope of our review or the studies were not randomised clinical trials. We listed the remaining 114 records, reporting on 114 studies, under studies awaiting classification because we could not be sure that these were randomised clinical trials from the information in the study paper. We could not obtain information on the registration of the study protocol for any of the 114 studies. We could not obtain information on study approval by regional research ethics committees, either from the study authors or through our own searches of trial registries. Corresponding authors did not respond to our enquiries about the design and conduct of the studies, except for one from whom we did not receive a satisfactory response. We also raised awareness of our concerns to editors of the journals that published the 114 studies, and we did not hear back with useful information. Moreover, there seemed to be inappropriate inclusion of trial participants, based on cancer stage and severity of liver disease, who should have obtained other interventions according to guidelines from learned societies.
We identified five ongoing trials, by handsearching in clinical trial websites.

Conclusions

We found no confirmed randomised clinical trials evaluating the combination of TACE plus thermal ablation versus TACE alone for people with hepatocellular carcinoma for inclusion in our review. Therefore, we cannot conclude anything on the treatment of hepatocellular carcinoma using TACE plus thermal ablation versus TACE alone.

We need trials that compare the beneficial and harmful effects of the combination of TACE plus thermal ablation versus TACE alone in people with hepatocellular carcinoma, not eligible for treatments with curative intent (liver transplantation, ablation surgical resection) and who have sufficient liver reserve, as assessed by the Child Pugh score, and who do not have extrahepatic metastases. Therefore, future trial participants must be classified at Barcelona Clinic Liver Cancer Stage B (intermediate stage) (BCLC-B) or an equivalent, with other staging systems.

Authors' conclusions

Implications for practice

No eligible randomised clinical trials assessing the beneficial and harmful effects of the combination of TACE plus thermal ablation versus TACE alone were included into this review. Therefore, our results did not show or reject the efficiency of any treatment strategy for hepatocellular carcinoma.

Implications for research

Large prospectively registered trials with rigorous methods comparing the beneficial and harmful effects of the combination of TACE plus thermal ablation versus TACE alone in hepatocellular carcinoma are needed. Such randomised clinical trials should be designed according to the SPIRIT statement (Chan 2013); registered in a WHO data register; with obtained full ethical approval; and reported according to the CONSORT statement (Schulz 2010). Such trials should be conducted in people who are not eligible for treatments with curative intent (liver transplantation, ablation surgical resection), who have sufficient liver reserve as assessed by the Child Pugh score, and do not have extrahepatic metastases. Therefore, future trial participants must be classified at Barcelona Clinic Liver Cancer Stage B (intermediate stage) (BCLC-B) or an equivalent, with other staging systems.

In view of the large number of studies we have identified as potentially problematic, there is an urgent need for validated tools to assist systematic review teams in identifying problematic studies. Our approach to assessing the 114 studies identified through electronic searching reinforces the importance of systematic review teams carefully appraising the studies they identify in order to reduce the impact of potentially problematic studies on evidence used to inform healthcare decision-making.

L'association de la chimioembolisation (CHE) et de l'ablation thermique par rapport à la CHE seule dans le carcinome hépatocellulaire

Contexte

Le carcinome hépatocellulaire (CHC) est une forme courante de cancer du foie: c'est le sixième cancer le plus fréquent dans le monde. La chimioembolisation (CHE) consiste à

injecter des agents dans les vaisseaux nourriciers de la tumeur afin de réduire l'apport sanguin vers celle-ci et de la détruire. Bien qu'il s'agisse du traitement le plus courant du CHC, les résultats cliniques sont médiocres. Au cours des dernières années, l'association de la CHE et de l'ablation thermique (destruction de la cellule tumorale en produisant de la chaleur ou du froid) s'est avérée plus efficace que la CHE seule. Cependant, les données probantes des effets bénéfiques ou des risques de l'association de la CHE et de l'ablation thermique chez les personnes atteintes d'un CHC demeurent toujours insuffisantes.

Objectif

Nous avons cherché à évaluer les effets bénéfiques et les risques de l'association de la CHE et de l'ablation thermique par rapport à la CHE seule contre le CHC.

Principaux résultats

Nous avons considéré 135 articles éligibles pour une analyse de texte intégral. Nous avons exclu 21 de ces articles car les interventions utilisées n'entraient pas dans le cadre de notre revue ou que les études n'étaient pas des essais cliniques randomisés. Nous avons répertorié les 114 articles restants, rapportant 114 études, dans la catégorie des études en attente de classification car nous ne pouvions pas établir avec certitude, à partir des informations contenues dans les documents, qu'il s'agissait d'essais cliniques randomisés. Nous n'avons pu obtenir d'informations sur l'enregistrement du protocole d'étude pour aucune des 114 études. Nous n'avons pas pu obtenir d'informations concernant l'approbation des études par les comités régionaux d'éthique de la recherche, que ce soit auprès des auteurs des études ou par nos propres recherches dans les registres d'essais. Les auteurs concernés n'ont pas répondu à nos demandes de renseignements sur la conception et la réalisation des études, à l'exception d'un seul dont la réponse n'a pas été satisfaisante. Nous avons également fait part de nos préoccupations aux rédacteurs en chef des revues qui ont publié les 114 études, mais nous n'avons pas reçu d'informations utiles en retour. De plus, il semble que des participants qui auraient dû bénéficier d'autres interventions conformément aux recommandations des sociétés savantes ont été inclus dans l'essai de façon inopportune, vis à vis du stade du cancer et de la gravité de la maladie hépatique.

Nous avons identifié cinq essais cliniques en cours, en effectuant une recherche manuelle sur les sites internet répertoriant les essais cliniques.

Conclusions

Nous n'avons pas trouvé d'essai clinique randomisé confirmé évaluant l'association de la CHE et de l'ablation thermique par rapport à la CHE seule chez les personnes atteintes d'un CHC à inclure dans notre revue. Par conséquent, nous ne pouvons pas

tirer de conclusion sur le traitement du CHC en recourant à la CHE associée à l'ablation thermique par rapport à la CHE seule.
Nous avons besoin d'essais comparant les effets bénéfiques et les risques de l'association de la CHE et de l'ablation thermique par rapport à la CHE seule chez les personnes atteintes d'un CHC, non éligibles aux traitements à visée curative (transplantation hépatique, ablation, résection chirurgicale) et dont la fonction hépatique est préservée, telle qu'évaluée par le score de Child-Pugh, et qui ne présentent pas de métastases extra-hépatiques. Par conséquent, les futurs participants à l'essai doivent être classés au stade B (stade intermédiaire) de la classification BCLC (Barcelona Clinic Liver Cancer) ou à un stade équivalent avec d'autres systèmes de classification.

Citation : Liu B, Zhang Y, Chen H, Li W, Tsochatzis E. The combination of transcatheter arterial chemoembolisation (TACE) and thermal ablation versus TACE alone for hepatocellular carcinoma. Cochrane Database of Systematic Reviews 2022, Issue 1. Art. No.: CD013345. DOI: 10.1002/14651858.CD013345.pub2.
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013345.pub2/full/fr#CD013345-abs-0013

4- Interventions for dialysis patients with hepatitis C virus (HCV) infection

What is the issue?

Hepatitis C is a disease of the liver caused by the hepatitis C virus (HCV) which spreads from person to person through blood contact, a result of sharing drug needles and other items contaminated with blood. This virus remains in the body for a long time, and in some it can affect the liver, causing its slow destruction or cirrhosis and liver cancer. Infected people may have weakness, nausea, jaundice and lose weight, and they may have increased liver enzymes and bilirubin.
HCV is present worldwide and varies amongst countries with a total of approximately 70 million people having a chronic infection and constitutes 40% of patients with chronic liver disease. People who are on haemodialysis for long periods have a higher chance of getting this infection. Direct-acting antiviral drugs, which can be taken by mouth, have replaced the previously used interferons for the treatment of HCV infection. Direct-acting antivirals have better efficacy and tolerability and are effective in almost all patients. The interferons have to be given as injections under the skin and have less efficacy and more side effects. Treatment with direct-acting antivirals has to be given for 12 weeks as compared to interferons which had to be given for at least 24 to 48 weeks with or without tablets of ribavirin to improve their efficacy. However, ribavirin can accumulate in kidney patients and cause the destruction of red blood cells and anaemia.

What did we do?

Since the publication of our previous review in 2015, newer medicines (direct-acting antivirals) for the treatment of HCV infection have become available, therefore, we have now updated the evidence to include the efficacy of direct-acting antivirals. This update searched for new evidence from randomised controlled studies for the treatment of HCV in dialysis patients.

What did we find?

The update found three studies with about 600 patients which could be included in addition to the previous review which had 10 studies all in haemodialysis. The use of the direct-acting antivirals grazoprevir and elbasvir in combination produces a 100% response by the end of treatment, but follow-up data is not available, and evidence is not of high quality. The addition of ribavirin to interferon resulted in a better sustained response (being free of the virus in blood after treatment is stopped), decreased chances of disease relapse but more adverse events. Telaprevir along with ribavirin in different doses combined with pegylated (PEG) interferon in different doses and durations produce almost similar end-of-treatment and sustained response, but the evidence was not of high quality. PEG interferon was more effective than standard interferon in producing a short-term response but not a sustained one and both were equally tolerated. Increasing the dose of PEG interferon did not improve response but was tolerated. Limitations of this review are that only a few studies were available with few participants, and patients with serious disease were excluded from previous studies in anticipation of side effects. Hence, the evidence available was not of high quality. Evidence for the newer medicines namely direct-acting antivirals which have now replaced the use of interferons in the general population was limited and was not of high quality.

Conclusions

This was an update of a review of available treatments for patients on dialysis having HCV infection. Direct-acting antivirals have now replaced the use of interferons for treatment. Grazoprevir and elbasvir produce an end-of-treatment response in almost all patients, but no data is available for a sustained response at follow-up, and the evidence is not of high quality. Combinations of telaprevir, ribavirin and PEG interferon used in different doses and durations are almost similar in efficacy, and the evidence is not of high quality. PEG interferon is more effective than standard interferon for producing a response by the end of treatment which is not sustained, both being equally tolerated. Increasing doses of PEG interferon does not improve responses, but high and low doses are equally tolerated. The addition of ribavirin produces an improved response even after stopping treatment but has higher adverse events.

Authors' conclusions

Implications for practice

Hepatitis C causes morbidity and death in CKD patients on dialysis and has implications for kidney transplant candidates. This review highlights the small number of studies with only a small number of participants available in most studies. There is a lack of high-quality evidence in this area, though direct-acting antivirals are the current preferred choice of therapy over interferons.

A combination of direct-acting antivirals grazoprevir and elbasvir produces end-of-treatment responses in nearly all patients and was well tolerated, although the certainty of the evidence is low.

A combination of PEG interferon and ribavirin produces an SVR, with lesser relapses with higher adverse events; the addition of telaprevir produced an end-of-treatment response and SVR irrespective of the dose of ribavirin or the duration of therapy.

Standard interferon produces an end-of-treatment response which is not sustained but is relatively well tolerated. PEG interferon is better than standard interferon in producing end-of-treatment but not SVR. Both are equally tolerated. Increasing doses of PEG interferon does not improve responses but is tolerated.

Implications for research

This review identifies the potential for conducting further RCTs using direct-acting antivirals in dialysis patients and testing SVR as a surrogate for long-term outcomes.

Interventions auprès des patients dialysés infectés par le virus de l'hépatite C (VHC)

Quelle est la problématique ?

L'hépatite C est une maladie du foie causée par le virus de l'hépatite C (VHC) qui se transmet d'une personne à l'autre par contact avec le sang, à la suite du partage de seringues et d'autres objets contaminés par le sang. Ce virus reste longtemps dans l'organisme et peut affecter le foie chez certains, provoquant sa lente destruction ou une cirrhose et un cancer du foie. Les personnes infectées pourraient présenter une faiblesse, des nausées, une jaunisse et une perte de poids, ainsi qu'une augmentation des enzymes hépatiques et de la bilirubine.

Le VHC est présent dans le monde entier et varie d'un pays à l'autre. Au total, environ 70 millions de personnes sont atteintes d'une infection chronique et représentent 40 % des patients souffrant d'une maladie hépatique chronique. Les personnes qui sont sous hémodialyse pendant de longues périodes ont un risque plus élevé de contracter cette infection. Les médicaments antiviraux à action directe, qui peuvent être pris par voie orale, ont remplacé les interférons précédemment utilisés pour le traitement de l'infection par le VHC. Les antiviraux à action directe ont une meilleure efficacité et

tolérabilité et sont efficaces chez presque tous les patients. Les interférons doivent être administrés sous forme d'injections sous la peau et sont moins efficaces et présentent davantage d'effets secondaires. Le traitement par antiviraux à action directe doit être administré pendant 12 semaines, alors que les interférons doivent être administrés pendant au moins 24 à 48 semaines, avec ou sans comprimés de ribavirine, afin d'améliorer leur efficacité. Cependant, la ribavirine peut s'accumuler dans les reins des patients et provoquer la destruction des globules rouges et une anémie.

Comment avons-nous procédé ?

Depuis la publication de notre précédente revue en 2015, de nouveaux médicaments (antiviraux à action directe) pour le traitement de l'infection par le VHC sont devenus disponibles, par conséquent, nous avons maintenant mis à jour les données probantes pour inclure l'efficacité des antiviraux à action directe. Cette mise à jour a recherché de nouvelles données probantes issues d'études contrôlées randomisées pour le traitement du VHC chez les patients dialysés.

Qu'avons-nous trouvé ?

La mise à jour a permis de trouver trois études portant sur environ 600 patients qui ont pu être incluses en plus de la revue précédente qui comportait 10 revues portant toutes sur l'hémodialyse. L'utilisation des antiviraux à action directe grazoprevir en association à elbasvir permet d'obtenir une réponse de 100 % à la fin du traitement, mais les données de suivi ne sont pas disponibles et les données probantes ne sont pas de grande qualité. L'ajout de la ribavirine à l'interféron a permis d'obtenir une réponse plus durable (absence de virus dans le sang après l'arrêt du traitement), de réduire les risques de rechute de la maladie, mais de provoquer davantage d'événements indésirables. Le télaprévir associé à la ribavirine à différentes doses et à l'interféron pégylé (PEG) à différentes doses et durées produisent des réponses presque similaires et durables en fin de traitement, mais les données probantes n'étaient pas de grande qualité. Le PEG interféron a été plus efficace que l'interféron standard pour produire une réponse à court terme, mais pas une réponse durable et les deux ont été équitablement tolérés. L'augmentation de la dose de PEG interféron n'a pas amélioré la réponse mais a été tolérée. Les limites de cette revue sont que seules quelques revues étaient disponibles avec peu de participants et que les patients atteints d'une maladie grave ont été exclus des études précédentes en prévision d'effets secondaires. Les données probantes disponibles n'étaient donc pas de grande qualité. Les données probantes concernant les nouveaux médicaments, à savoir les antiviraux à action directe, qui ont désormais remplacé l'utilisation des interférons dans la population générale, étaient limitées et n'étaient pas de grande qualité.

Conclusions

Il s'agit d'une mise à jour d'une revue des traitements disponibles pour les patients sous dialyse atteints d'une infection par le VHC. Les antiviraux à action directe ont désormais remplacé l'utilisation des interférons pour le traitement. Le grazoprevir et l'elbasvir produisent une réponse en fin de traitement chez presque tous les patients, mais aucune donnée n'est disponible pour une réponse durable lors du suivi et les données probantes ne sont pas de grande qualité. Les associations de télaprévir, de ribavirine et d'interféron PEG utilisées à des doses et des durées différentes ont une efficacité presque similaire mais les données probantes ne sont pas de grande qualité. L'interféron PEG est plus efficace que l'interféron standard pour produire une réponse à la fin du traitement qui n'est pas durable, les deux étant équitablement tolérés. L'augmentation des doses de PEG interféron n'améliore pas les réponses, mais les doses faibles et élevées sont équitablement tolérées. L'ajout de ribavirine permet d'obtenir une meilleure réponse même après l'arrêt du traitement, mais les événements indésirables sont plus nombreux.

Citation : Prabhu AR, Rao IR, Nagaraju SP, Rajwar E, Venkatesh BT, Nair N S, Pai G, Reddy NP, Suvarna D. Interventions for dialysis patients with hepatitis C virus (HCV) infection. Cochrane Database of Systematic Reviews 2023, Issue 4. Art. No.: CD007003. DOI: 10.1002/14651858.CD007003.pub3. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD007003.pub3/full/fr#CD007003-abs-0010

5- Interventions for the long-term prevention of hereditary angioedema attacks

What is hereditary angioedema and how is it treated?

Hereditary angioedema (HAE) is a serious and potentially life-threatening condition that causes acute (sudden onset) attacks of swelling, pain and reduced quality of life. Several new medicines have been developed to treat acute attacks and prevent attacks from occurring. Some medicines are taken by mouth, whereas others are injected under the skin, or given by a vein directly into the blood.

The medicines currently given for preventing HAE attacks are human C1 esterase inhibitor (often abbreviated as C1-INH), berotralstat, lanadelumab, tranexamic acid, and danazol. In addition, we found a further medicine (avoralstat) that is currently being studied for its ability to prevent HAE attacks.

What did we want to find out?

We investigated whether these medicines reduce the number of HAE attacks, and if any attacks that do occur are less severe than they would otherwise be. We also looked at whether people taking the medicines experienced a better quality of life, and whether the medicines caused unwanted side effects.

What did we do?

We searched medical databases for clinical studies in children or adults with HAE that compared medications to prevent HAE attacks with placebo (a pretend treatment) or another medicine.

What did we find?

We found 15 studies with 912 participants. All medicines except avoralstat reduced the number of HAE attacks, and even when attacks did occur, they were less severe for C1-INH and lanadelumab (there were no results for the other medicines). We found that most medicines improved the quality of life of the people with HAE and were generally safe as they did not increase the number of serious and less serious side effects.

We found no studies that tested tranexamic acid, and only one study tested danazol. There were also no studies that compared one medicine directly with another. This means that we cannot say for sure whether one medicine is better than another.

Conclusions

C1-INH, berotralstat, lanadelumab and danazol appear to reduce the risk of HAE attacks and increase the quality of life in people with HAE. The medicines do not seem to result in an increase in side effects.

What are the limitations of the evidence?

Our findings are limited by the small number of studies and the small number of participants in each study. Therefore, our confidence in these findings is low.

How up to date is this evidence?

The evidence is current to 3 August 2021.

Authors' conclusions

Implications for practice

Our data show that there is an evidence base for the use of avoralstat, C1 esterase inhibitor (C1-INH; in various forms), lanadelumab and danazol in preventing hereditary angioedema (HAE) attacks. We were unable to find any studies of the use of tranexamic acid in preventing attacks. Current data show that avoralstat is ineffective in preventing attacks, whereas the other drugs (C1-INH, danazol, lanadelumab, berotralstat) demonstrated efficacy. All drugs for which data were available (avoralstat, berotralstat, C1-INH (in all forms), and lanadelumab), do not appear to increase the risk of adverse events including serious adverse events. However, the implications for practice resulting from our analysis are limited. There are insufficient studies available to draw firm conclusions about the absolute or relative efficacy of any drug compared with placebo or an active comparator. It is possible that danazol, subcutaneous C1-INH and recombinant human C1-INH are more effective than berotralstat and lanadelumab in reducing the risk of

breakthrough attacks, but the small number of studies and the small size of the studies means that the certainty of the evidence is low. This and the lack of head-to-head trials prevented us from drawing firm conclusions on the relative efficacy of the drugs. No studies were available in people with Type III HAE, and as such, we can provide no conclusions about the efficacy or safety (or both) of interventions for this HAE type.

Implications for research

This analysis has highlighted the need for further investigation of all drugs for the prevention of HAE. We did not find a single trial that compared any drug with another drug. Both patients and clinicians need to know which drug is most effective and safest; the current data do not allow us to draw firm conclusions about the relative efficacy or safety of the various drugs available to patients. Furthermore, studies are needed in people with Type III HAE, and in populations of differing genetic and cultural backgrounds.

We are cognisant of the fact that the rarity of HAE makes such trials difficult and expensive, and the rarity of the condition makes manufacturers less willing to invest in the conditions. We therefore hope that a national or international funding agency will see the urgent requirement for clarity in this area, and assist with sufficient funding to provide more certainty for both patients and their doctors.

Interventions de prévention à long terme des crises d'angio-œdème héréditaire

Qu'est-ce que l'angio-œdème héréditaire et comment est-il traité ?

L'angio-œdème héréditaire (AOH) est une maladie grave et potentiellement mortelle qui provoque des crises aiguës (d'apparition soudaine) de gonflement, de douleur et de réduction de la qualité de vie. Plusieurs nouveaux médicaments ont été mis au point pour traiter les crises aiguës et prévenir les crises. Certains médicaments sont pris par voie orale, tandis que d'autres sont injectés sous la peau, ou administrés par une veine directement dans le sang.

Les médicaments actuellement administrés pour prévenir les crises d'AOH sont l'inhibiteur de la C1 estérase humaine (souvent abrégé en C1-INH), le berotralstat, le lanadelumab, l'acide tranexamique et le danazol. Par ailleurs, nous avons trouvé un autre médicament (l'avoralstat) dont la capacité à prévenir les crises d'AOH est actuellement en cours d'étude.

Que voulions-nous découvrir ?

Nous voulions savoir si ces médicaments réduisent le nombre de crises d'AOH et si les crises qui se produisent sont moins graves qu'elles ne le seraient autrement. Nous voulions aussi savoir si les personnes prenant les médicaments avaient une meilleure qualité de vie et si les médicaments avaient des effets secondaires indésirables.

Comment avons-nous procédé ?

Nous avons recherché dans les bases de données médicales les études cliniques menées chez des enfants ou des adultes atteints d'AOH qui comparaient les médicaments destinés à prévenir les crises d'AOH à un placebo (un traitement fictif) ou un autre médicament.

Qu'avons-nous trouvé ?

Nous avons trouvé 15 études avec 912 participants. Tous les médicaments, à l'exception de l'avoralstat, ont réduit le nombre de crises d'AOH, et même lorsque des crises se produisaient, elles étaient moins graves avec le C1-INH et le lanadelumab (aucun résultat pour les autres médicaments). Nous avons constaté que la plupart des médicaments amélioraient la qualité de vie des personnes atteintes d'AOH et étaient généralement sûrs car ils n'augmentaient pas le nombre d'effets secondaires graves et moins graves.

Nous n'avons trouvé aucune étude sur l'acide tranexamique, et une seule étude évaluant le danazol. Il n'y avait pas non plus d'études comparant directement un médicament à un autre. Cela signifie que nous ne pouvons pas affirmer avec confiance qu'un médicament est meilleur qu'un autre.

Conclusions

Le C1-INH, le berotralstat, le lanadelumab et le danazol réduiraient le risque de crises d'AOH et amélioreraient la qualité de vie des personnes atteintes d'AOH. Les médicaments ne semblent pas entraîner une augmentation des effets secondaires.

Quelles sont les limites des données probantes ?

Nos conclusions sont limitées par le faible nombre d'études et le faible nombre de participants dans chaque étude. Ainsi, le niveau de confiance de ces résultats est faible.

Ces données probantes sont-elles à jour ?

Les données probantes sont à jour jusqu'au 3 août 2021.

Citation : Beard N, Frese M, Smertina E, Mere P, Katelaris C, Mills K. Interventions for the long-term prevention of hereditary angioedema attacks. Cochrane Database of Systematic Reviews 2022, Issue 11. Art. No.: CD013403. DOI: 10.1002/14651858.CD013403.pub2. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013403.pub2/full/fr#CD013403-abs-0012

6- Vitamin D supplementation for chronic liver diseases in adults

Review question

Is vitamin D supplementation beneficial or harmful for adults with chronic liver diseases?

Background

The available evidence on vitamin D and chronic liver diseases in adults is inconclusive. The aim of this systematic review (a summary of results of available healthcare trials) was to analyse the benefits and harms of the different forms of vitamin D in people with chronic liver diseases.

Study characteristics

Twenty-seven trials with 1979 adult participants provided data for this review. This review update added 12 trials with 945 participants. The 1979 trial participants were randomly assigned to vitamin D compared with placebo (dummy pill) or no treatment. Eleven trials were conducted in high-income countries, and 16 trials in middle-income countries. The age range of the participants was 28 years to 61 years, and on average 44% were women. Ten trials included people with chronic hepatitis C, five trials people with liver cirrhosis, 11 trials people with non-alcoholic fatty liver disease, and one trial liver transplant recipients. There were no trials including people with chronic hepatitis B or inherited liver diseases. All of the included trials reported the baseline vitamin D status of participants. Vitamin D administration lasted on average six months, and most trials used the cholecalciferol (vitamin D_3) form.

Funding

Fourteen trials appeared to be free of vested interest that could bias the trial results. Eleven trials may not have been free of vested interest, as they did not provide any information on clinical trial support or sponsorship. Two trials were funded by industry. We found no difference between trials without industry support compared to trials at risk of industry support in our analysis.

Key results

There is not enough evidence to determine whether vitamin D has beneficial or harmful effects, or has little to no effect on chronic liver diseases in adults. There were too few participants in the individual trials as well as in our evidence synthesis. The trials were at high risk of bias so we lack fair assessments of the benefits and harms of vitamin D in this population. Neither benefits nor harms of vitamin D supplementation in people with chronic liver diseases can be excluded. There were no trials including people with chronic hepatitis B and inherited liver diseases.

Quality of the evidence

We judged all trials to be at high risk of bias (that is an underestimation or overestimation of the true intervention effect). The certainty of evidence is very low.

Currentness of evidence

The evidence is current to November 2020.

Authors' conclusions

Implications for practice

Based on trials with very low certainty of evidence, vitamin D supplementation versus placebo or no intervention may increase or reduce all-cause mortality, liver-related mortality, serious adverse events, and non-serious adverse events in adults with chronic liver diseases. Evidence on the effect of vitamin D supplementation on liver-related morbidity such as gastrointestinal bleeding, hepatic encephalopathy, hepatorenal syndrome, ascites, or liver cancer, and on health-related quality of life is lacking. Our conclusions are based on trials at high risk of bias, with an insufficient number of participants, and on a lack of trial data on clinically important outcomes. In addition, the analysed trials showed significant intertrial heterogeneity for some outcomes.

Implications for research

More evidence is needed before any final conclusions can be drawn on the effect of vitamin D on chronic liver diseases, especially in people with cholestatic and autoimmune liver diseases. There is also a need for trials evaluating vitamin D supplementation versus placebo or no intervention in people with chronic hepatitis C, chronic hepatitis B, and autoimmune liver diseases. More randomised clinical trials assessing a longer duration of vitamin D intervention and different forms of vitamin D with a greater number of participants, assessing clinical outcomes, seem appropriate. The effect of vitamin D on health-related quality of life also deserves further investigation. Future trials should be designed according to the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) statement (www.spirit-statement.org/) and reported according to the CONSORT statement (www.consort-statement.org).

Supplémentation en vitamine D dans les maladies hépatiques chroniques chez les adultes

Problématique de la revue

La supplémentation en vitamine D est-elle bénéfique ou néfaste pour les adultes atteints de maladies chroniques du foie ?

Contexte

Les données probantes disponibles sur la vitamine D et les maladies chroniques du foie chez les adultes ne sont pas concluantes. L'objectif de cette revue systématique (un résumé des résultats des essais de soins de santé disponibles) était d'analyser les bénéfices et les risques des différentes formes de vitamine D chez les personnes atteintes de maladies chroniques du foie.

Caractéristiques des études

Vingt-sept essais avec 1979 participants adultes ont fourni des données pour cette revue. Cette mise à jour de la revue nous a permis d'ajouter 12 essais avec 945 participants. Les 1979 participants à l'essai ont été répartis au hasard entre la vitamine D, un placebo (pilule factice) ou l'absence de traitement. Onze essais ont été menés dans des pays à revenu élevé, et 16 dans des pays à revenu intermédiaire. La fourchette d'âge des participants allait de 28 ans à 61 ans, et en moyenne 44 % étaient des femmes. Dix essais portaient sur des personnes atteintes d'hépatite C chronique, cinq essais sur des personnes atteintes de cirrhose hépatique, onze essais sur des personnes atteintes de stéatose hépatique non alcoolique et un essai sur des transplantés du foie. Il n'y a pas eu d'essais incluant des personnes atteintes d'hépatite B chronique ou de maladies hépatiques héréditaires. Tous les essais inclus ont mesuré et rapporté les valeurs initiales de vitamine D des participants. L'administration de vitamine D a duré en moyenne six mois, et la plupart des essais ont utilisé la forme cholécalciférol (vitamine D_3).

Financement

Quatorze essais ont semblé être exempts d'intérêts particuliers susceptibles de biaiser les résultats de l'essai. Onze essais pourraient ne pas avoir été exempts d'intérêts particuliers, car ils n'ont pas fourni d'information sur le soutien ou le financement des essais cliniques. Deux essais ont été financés par l'industrie. Dans notre analyse, nous n'avons pas trouvé de différence entre les essais sans soutien de l'industrie et les essais à risque de soutien de l'industrie.

Principaux résultats

Il n'y a pas suffisamment de données probantes pour déterminer si la vitamine D a des effets bénéfiques ou nocifs, ou si elle a peu ou pas d'effet sur les maladies chroniques du foie chez les adultes. Il y avait trop peu de participants dans les essais individuels ainsi que dans notre synthèse des données probantes. Les essais présentaient un risque élevé de biais et nous ne disposons donc pas d'évaluations justes des bénéfices et des risques de la vitamine D dans cette population. On ne peut exclure ni les bénéfices ni les risques d'une supplémentation en vitamine D chez les personnes atteintes de maladies chroniques du foie. Il n'y a pas eu d'essais incluant des personnes atteintes d'hépatite B chronique et de maladies hépatiques héréditaires.

Qualité des données probantes

Nous avons jugé que tous les essais présentaient un risque élevé de biais (c'est-à-dire une sous-estimation ou une surestimation de l'effet réel de l'intervention). Le niveau de confiance des données probantes est très faible.

Les données probantes sont-elles à jour ?

Les données probantes sont à jour jusqu'en novembre 2020.

Citation : Bjelakovic M, Nikolova D, Bjelakovic G, Gluud C. Vitamin D supplementation for chronic liver diseases in adults. Cochrane Database of Systematic Reviews 2021, Issue 8. Art. No.: CD011564. DOI: 10.1002/14651858.CD011564.pub3.
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD011564.pub3/full/fr#CD011564-abs-0010

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https://www.afro.who.int/fr/regional-director/speeches-messages/journee- mondiale-contre-lhepatite-2023