Antioxidant supplementation for liver disease

By Hanan Khalil

Objectives

The purpose of this evidence summary is to present the best available evidence for the effectiveness and adverse effects of antioxidant supplementation for the treatment of acute and chronic liver disease based on a systematic review by the Cochrane Collaboration. For the full review see: http://dx.doi.org/10.1002/14651858.CD007749.pub2

Background

Oxidative stress is defined as an imbalance between oxidants and antioxidants in favour of the oxidants potentially leading to damage and disturbances in the normal state of tissue through the production of peroxidises and free radicals. Oxidative stress has been implicated as having an important pathogenic role in alcoholic liver disease, viral hepatitis, non-alcoholic steatohepatitis, autoimmune liver disease, liver cancer and liver cirrhosis. Several studies addressed antioxidant supplementation for patients with various conditions such as non-alcoholic fatty liver diseases, alcoholic liver disease, and hepatitis B or C virus liver disease with inconclusive results.

Characteristics of studies

Study participants

The participants selected for the systematic review included adults (18 years and over) with autoimmune liver disease, viral hepatitis, alcoholic liver disease and cirrhosis of any aetiology. Participants with special dietary needs, pregnant and lactating women and people with malignant liver disease were excluded.

Interventions

The interventions considered in the review included studies that compared antioxidant supplements such as beta-carotene, vitamin A, vitamin C, vitamin E and selenium at any dose, duration and route of administration compared to placebo or no intervention. The antioxidant supplements were administered either singly, or in combination among themselves or with other vitamins and trace elements. Several outcomes were addressed in the review. These were divided into primary and secondary outcomes. The primary outcomes measure included all-cause mortality, liver-related mortality and liver-related morbidity such as liver cancer, gastrointestinal bleeding, liver encephalopathy, hepato-renal syndrome, ascites and jaundice, adverse effects and quality of life measures. Secondary outcome measures included biochemical indices such as ALT, AST, bilirubin and albumin and failure of virological response at the end of treatment and six months after treatment.

Studies included

Twenty studies were included with a total of 1,225 participants. Seven studies had patients with alcoholic liver disease, nine studies had patients with chronic hepatitis C, two studies had patients with chronic hepatitis B, one study had patients with primary biliary cirrhosis and one study in patients with liver cirrhosis. The doses for the supplements used in this review were as follows: beta-carotene 6 to 40 mg, vitamin A 5,000 to 10,000 mcg, vitamin C 120 mg to 3,000 mg, vitamin E 30 to 1,000 IU, and selenium 100 to 400 mcg. The duration of supplementation varied from one day to five years with a mean duration of 0.75 years, and the duration of follow up ranged from one day to eight years with a mean duration of 1.1 years.

Quality of the research

All studies included in the systematic review were randomised controlled trials (RCTs) in which all participants had liver disease. Only five studies were considered as having low risk of bias by the authors. Various pharmaceutical companies provided the antioxidant supplements in at least ten studies of the twenty reported in the systematic review.

Results

- The supplementation of antioxidants had no significant effect on all cause mortality with a RR of 0.88 and a CI ranging between 0.60 and 1.19.
- The antioxidant supplements had no clinical significant effect on liver-related mortality and morbidity between the intervention and the control group.
- Several adverse effects such as dyspepsia, fatigue, leukocytopenia, thrombocytopenia and autoimmune thyroiditis were reported by the participants in the intervention group, but none of them were clinically significant.
- Only one study reported on quality of life measures. There was no clinical significance between the intervention and the control groups in outcomes measured pre and post treatment.
- There were also no significant effects on the activity of AST, albumin and bilirubin between the intervention and the control groups. Only a moderate significance was observed in ALT levels depending on the type of analysis used (fixed rate vs random effect meta-analysis).
• The antioxidant supplements had no significant effect on end of treatment virological response in patients with chronic viral hepatitis (A, B and C).

Implications for research

The lack of the uniformity in reporting the various outcomes in randomised controlled trials contributes to the difficulty in pooling the results of various RCTs. Researchers are encouraged to adopt the Consolidated Standards of Reporting trials in order to easily compare studies with similar outcomes.

Conclusion

There is lack of compelling evidence supporting the use of antioxidant supplements for patients with autoimmune, alcoholic, acute and chronic hepatits B or C virus liver diseases or liver cirrhosis.

References