

Does milk thistle do any good?



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Self-treating pharmacist with hepatitis B inspires a deep dive into the limited literature

CLINICAL SCENARIO

Thanh, a 35-year-old pharmacist with chronic hepatitis B, consulted me recently.

He mentioned that he had been treating himself with a milk thistle (*Silybum marianum*) product and wondered what my thoughts about it were.

I knew milk thistle was commonly marketed for “liver health” and wondered what the evidence was.

CLINICAL QUESTION

What is the effect of milk thistle extract on liver disease severity in people with chronic hepatitis B?

THE RESEARCH EVIDENCE

STEP 1: The Cochrane Library

The library has a systematic review, updated to 2005, on milk thistle for alcoholic and/or hepatitis B or C virus liver diseases.¹

STEP 2: TripDatabase

I conducted a search using the PICO search tool (Participant: “hepatitis B”, Intervention: “milk thistle”, Comparator: “placebo”, Outcomes: blank). There did not appear to be a more appropriate or newer paper. TripDatabase did identify two newer studies in patients with viral hepatitis. However, one was in patients with chronic hepatitis C² and the other was terminated with no results available.

Although it isn't ideal, let's look at the Cochrane systematic review by Rambaldi et al (2007)³ in detail.

CRITICAL APPRAISAL

I will use the systematic review's critical appraisal sheet from the Centre for Evidence Based Medicine.³

PICO

WHAT PICO QUESTION DOES THE SYSTEMATIC REVIEW ASK?

In people living with alcoholic liver disease, and/or viral induced liver diseases (hepatitis B and/or C) (Participants); what is the effect of milk thistle or any milk thistle constituent at any dose or duration (Intervention); compared with placebo or no intervention (Comparator); on several outcome measures including, (i) death, (ii) development of hepatitis clinical symptoms and complications (e.g. ascities, variceal bleeding), (iii) liver biochemistry, (iv) liver biopsy findings, and (v) adverse events (Outcome).

IS IT CLEARLY STATED?

Yes.

IS IT UNLIKELY THAT IMPORTANT STUDIES WERE MISSED?

Unclear. Although the authors searched multiple electronic databases and approached the principal authors of the identified trials and the manufacturers of milk thistle products to inquire about any relevant unidentified or unpublished randomised trials, this systematic review is close to 12 years out of date.

WERE THE CRITERIA USED TO SELECT ARTICLES FOR INCLUSION APPROPRIATE?

Yes. The authors included only randomised trials that enrolled patients with the aforementioned types of liver disease. Other types of liver disease, and trials of liver disease prevention, were excluded.

WERE THE INCLUDED STUDIES SUFFICIENTLY VALID FOR THE QUESTION ASKED?

Unclear, possibly not. The authors formally assessed the risk of bias of the



included studies using a clearly described process (pp 4-5).¹ Of the 13 included trials, only one provided a sample size calculation (see Stat Facts), six had an adequate method to generate the allocation sequence, only three described adequate allocation concealment – with only one described as double-blinded.

WERE THE RESULTS SIMILAR BETWEEN STUDIES?

Mostly. There was little heterogeneity in the results as presented, though given the small number of studies, there were not many direct comparisons.

THE RESULTS

The results are very limited. Of the included studies, only one was specifically in people with hepatitis B, and there were fewer than 30 participants in that study. Participants who received milk thistle compared with placebo:

- There was no difference in mortality (analysis 1.1, p 39) or liver-related mortality (analysis 2.1, p 53). Note: there were no deaths in the studies of participants with viral hepatitis.
- There were no differences in the risk of any liver complications (analysis 3.4, p 59). Note: results for people with HBV not available.
- There was no effect on fibrosis score (analysis 3.13, p 67). Note: single study in alcoholic liver disease.

DISCUSSION AND CONCLUSION

There is limited evidence about the effect of milk thistle on liver diseases generally, and on chronic hepatitis B specifically.

Of the evidence that exists, the quality appears to be low, with most of the randomised trials having small numbers of participants and methodological issues.

When all the trials are taken together, there was a statistically significant

beneficial effect on liver-related mortality, but this was mostly in the alcoholic-liver disease participants and the benefit was no longer statistically significant when the analysis was restricted to high-quality studies.¹

My interpretation of the evidence is that it is insufficient to provide an estimate of the effect of milk thistle on chronic hepatitis B.

Of the evidence that does exist, there do not appear to be any dramatic beneficial effects, and the possibility that there are no meaningful therapeutic effects seems likely.

The precautionary principle should apply and milk thistle products cannot be recommended for chronic hepatitis B.

On further discussion with Thanh, he had not experienced any subjective benefit from milk thistle and was happy to stop using it. ■

References at medobs.com.au



Stat Facts

SAMPLE-SIZE CALCULATION

The sample-size of a clinical trial should be determined in the study design. This depends importantly on the expected magnitude of the effect (more participants are required to identify a smaller effect). Studies with too few participants have low statistical power and thus a lower chance of detecting a true effect. Less commonly appreciated is that low power also increases the risk that a positive result is false, and that the detected effect size is an overestimate.⁴