

HEPATOCELLULAR CARCINOMA

Vitamin K₂ does not prevent cancer recurrence

Despite potentially curative treatments such as surgical resection or radiofrequency ablation, hepatocellular carcinoma (HCC) often recurs. Vitamin K is thought to be involved in the control of cell growth, and an abnormal protein produced in vitamin K-deficient individuals is an HCC-specific tumor marker. However, small studies of the effects of vitamin K therapy on HCC recurrence have produced conflicting results. Researchers from Japan have now tested the effect of vitamin K₂ in a large, randomized, controlled trial. “Vitamin K₂ did not prevent recurrence of [HCC],” states Haruhiko Yoshida, the study’s corresponding author.



The participants in this multicenter, double-blind study were 548 patients who had undergone potentially curative treatment (local ablation or surgery) for HCC. They were randomly assigned to one of three treatment groups—placebo, vitamin K₂ 45 mg daily or vitamin K₂ 90 mg daily (twice the recommended dose for patients with osteoporosis). Patients were monitored for HCC recurrence using dynamic CT–MRI at 12-week intervals and by checking for HCC-specific markers every 4 weeks.

Interim analyses at 1 year and 2 years showed that vitamin K₂ treatment did not increase the incidence of adverse effects, but it did not prevent HCC recurrence or death either. The study was, therefore, terminated about 18 months after enrollment started.

Further analysis of data from the study confirmed the lack of any effect of vitamin K₂ on HCC recurrence. Subgroup analyses, in which the type of recurrence (intrahepatic metastasis versus *de novo* HCC) as well as various tumor-related

factors were considered, also produced negative results. As the exact effect of vitamin K on the growth of HCC cells is not clear, the researchers recommend caution with the administration of high-dose vitamin K to patients with HCC who are at high risk of intrahepatic recurrence.

Even though vitamin K₂ was previously reported to prevent the development of HCC, “...the effect of vitamin K on recurrence, if any, might be observed only in carefully selected patients in a very large-scale trial,” the researchers write. “Our study does not exclude this possibility. However, prevention of [HCC] recurrence ... is still a clinically very important issue [and] requires other approaches,” they conclude.

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Original article Yoshida, H. *et al.* Effect of vitamin K₂ on the recurrence of hepatocellular carcinoma: a randomized, placebo-controlled, double-blind phase II/III study. *Hepatology* doi:10.1002/hep.24430