

Folic Acid May Prevent Progression to Laryngeal Cancer

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ROME, June 12 — Folic acid supplements appear to prevent some laryngeal lesions from progressing to cancer, according to a small Italian pilot study.

In the non-randomized and uncontrolled study, Giovanni Almadori, M.D., of the Università Cattolica del Sacro Cuore here, and colleagues examined the effect of folate supplements - 5 mg every eight hours for six months - on 43 patients diagnosed with glottic laryngeal leucoplakia.

Patients were initially diagnosed with indirect laryngoscopy and the diagnosis was confirmed by diagnostic direct microlaryngoscopy and biopsy. Dr. Almadori and colleagues reported in the June 12 online issue of *Cancer*. During the study, patients were monitored every 30 days by videolaryngoscopy.

At baseline, the mean serum folate level was slightly more than five nanograms per milliliter and the mean serum homocysteine level was almost 11 micromol per liter. A folate deficiency is considered to be a level less than 3 mg/mL, although some studies have suggested that it should be 5 mg/mL.

The researchers found:

31 of the 43 patients had at least a 50% reduction in lesion size.

Of those, 12 responded completely, with no further indication of disease.

Over the six months, mean serum folate levels increased by 10.06 mg/mL and the mean homocysteine serum levels decreased by 3.65 micromol per liter. The changes were significant at $P < 0.0001$.

The histology of laryngeal leucoplakia lesions can range from normal mucosa to severe dysplasia, Dr. Almadori and colleagues noted. In this study, five of the patients began with normal mucosa, 11 with hyperplasia, and nine each with mild, moderate, or severe dysplasia.

Interestingly, patients with a more disturbed histology were more likely to have low folate levels and to respond to the supplements:

Of the five with normal histology, none responded.

There were five responses among the 11 with hyperplasia, including one complete response.

All of the patients with mild dysplasia responded, including two complete responses.

All but one of those with moderate dysplasia responded, including three complete responses.

And all of those with severe dysplasia responded, including six complete responses.

The response rate is lower than that seen in other chemopreventive studies, such as those using retinoids, but the toxicity is markedly lower, Dr. Almadori and colleagues noted; folate is a naturally occurring B-vitamin found in fruits and vegetables.

The finding opens "intriguing perspectives," said Dr. Almadori, because folate deficiency was reported in 2001 to be the main vitamin deficiency seen in the U.S. population.

"Folate supplementation, alone or in combination with other chemopreventive drugs, could effectively reduce the risk of progression in an already genetically altered mucosa, especially in patients with hypofolatemia," they suggested.

"Our results are encouraging because we obtained a complete response rate of 27% and never observed any clinical or histologic progression during a six-month treatment," Dr. Almadori and colleagues concluded.

However, they cautioned that no firm conclusions can be drawn because there are little data on the spontaneous regression of laryngeal leucoplakia. To fill that gap, the researchers are planning a randomized, double-blind trial.

Action Points

Advise interested patients that this small and uncontrolled study seems to suggest that folate supplements may be beneficial in patients with laryngeal leucoplakia.

Note that lack of folic acid was reported in 2001 to be the most common vitamin deficiency in the U.S.

Primary source: Cancer

Source reference:

Giovanni Almadori et al. "Pilot Phase IIA Study for Evaluation of the Efficacy of Folic Acid in the Treatment of Laryngeal Leucoplakia." *Cancer* 2006; 107: DOI: 10.1002/cncr.22003.