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Short Review Open Access

# Vitamin A, D, and E after Gastrectomy for Gastric Cancer

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Abnormal vitamin metabolism after gastric surgery for gastric cancer has been reported over the past 20 years. Castle factor deficiency after gastrectomy causes malabsorption of vitamin B12. The need for prophylaxis and treatment of vitamin B12 deficiency after gastrectomy is widely acknowledged by surgeons [1]. Fat malabsorption after gastrectomy for gastric cancer has already been documented [2], suggesting potential malabsorption of fat-soluble vitamins such as vitamin D (VD), vitamin A (VA), and vitamin E (VE) after operation. However, most surgeons are unaware of changes in VD, VA, and VE after gastrectomy for gastric cancer.

## Vitamin D

VD is synthesized in the skin in response to ultraviolet radiation and is also absorbed from the diet. It is then transported to the liver, where it undergoes 25-hydroxylation, resulting in the formation of 25-hydroxyvitamin D3. This metabolite is the major circulating form of VD. The final step in hormone activation, 1α-hydroxylation, occurs in the kidney [3]. Changes in serum VD levels after gastrectomy were reported in 2007 [4]. The serum level of $1,25(OH)_2VD$, the most active metabolite of VD, was found to be normal after gastrectomy in all 22 patients studied. The serum $1,25(OH)_2VD$ level did not decrease with time after gastrectomy and was unaffected by the type of gastrectomy procedure. In contrast, the serum level of 25(OH)VD, which is weakly active, was below the lower limit of normal in 7 (32%) of the 22 patients. One (17%) of the 6 patients tested less than 1 year postoperatively had a serum 25(OH)VD level below the normal range, versus 6 (38%) of the 16 patients tested 1 year or more after surgery, although the difference between the groups was not statistically significant. However, the mean serum level of 25(OH)VD was significantly lower in patients tested 1 year or more postoperatively than in those tested less than 1 year postoperatively (p=0.041) and was also significantly lower in patients who had received a total gastrectomy than in those who had received other gastrectomy procedures. The level of $24,25(OH)_2VD$, a weakly active metabolite of 25(OH)VD, was below the normal range in 19 (86%) of the 22 patients. The level of $24,25(OH)_2VD$ was below the normal range in 5 (83%) of 6 patients tested less than 1 year postoperatively, as compared with 14 (88%) of 16 patients tested 1 year or more postoperatively. Although the difference between the groups was not significant, one of the patients tested 1 year or more postoperatively had a $24,25(OH)_2VD$ level above the normal range. The mean $24,25(OH)_2VD$ level was slightly but not significantly lower in patients tested 1 year or more postoperatively than in those tested less than 1 year postoperatively, as was the case for 25(OH)VD. The mean $24,25(OH)_2VD$ level was slightly but not significantly lower in patients who had received a total gastrectomy.

The patients thus showed decreased serum levels of $25(OH)VD_3$ and $24,25(OH)_2VD_3$, which are weakly active metabolites of VD. This finding suggests that a homeostatic response maintains a normal level of $1,25(OH)_2VD_3$, which has a pivotal role in the regulation of calcium metabolism.

These data were obtained in Japanese patients. Studies in American patients have reported that the serum $25(OH)VD_3$ level decreased and the serum $1,25(OH)_2VD_3$ level increased after gastrectomy [5]. There may be racial differences in VD metabolism.

## Vitamins A and E

Since VE cannot be synthesized in the human body, VE absorption depends on dietary intake. Although there are eight kinds of natural VE analogues (i.e., four kinds of tocopherols and the corresponding tocotrienols), α-tocopherol is selectively retained in the body. VE, a fat-soluble vitamin, is absorbed in the intestine and binds to chylomicrons, lipoproteins synthesized in the intestine. It then appears in the lymph and is partially incorporated into the liver. In vivo α-tocopherol is identified and its serum concentration is maintained by α-tocopherol transport protein (α-TTP), which is excreted in the liver and stored in tissues [6,7]. VE deficiency can be caused by absorption and transport defects, as well as by impairment of the α-tocopherol identification process. Malabsorption and transport disorders include fat malabsorption [8-10], such as that associated with abetalipoproteinemia [11-13], congenital biliary atresia, and short bowel syndrome, and exocrine impairment [10], such as that occurring in cystic fibrosis. Identification defects include hereditary α-TTP abnormalities [13].

Malabsorption of various nutrients is attributable to environmental changes affecting digestion and absorption after gastric surgery for gastric cancer. Fat malabsorption after gastrectomy for gastric cancer has been reported [2]. Serum VA and VE levels decrease after gastrectomy for gastric cancer. Changes in serum VE and VA levels in patients who had previously undergone gastrectomy for gastric cancer were reported in 2007 [14,15]. In 12 (21.8%) of the 55 patients, serum VE levels decreased. In contrast, serum VA levels decreased in only 1 (1.8%) of 55 patients. The incidence of low VE levels in the total gastrectomy group (34.6%, 9/26) was significantly higher than that in the subtotal gastrectomy group (10.3%, 3/29; p=0.048). When serum VE levels were compared according to the reconstruction procedure, the proportion of patients with low VE levels was significantly higher in the group without food passage through the duodenum (34.4%, 11/32) than in the group with food passage through the duodenum (4.3%, 1/23; p=0.009). When serum VE levels were compared according to the time after gastrectomy, the interval after surgery in the low VE group (7.3 years) was significantly longer than that in the normal VE group (5.1 years; p=0.024).

Serum levels of VA and total cholesterol in the low VE group were significantly lower than those in the normal or high VE group. In addition, white cell count was significantly higher in the low VE group than in the normal or high VE group. The serum total cholesterol level significantly correlated with the serum VE level (r=0.697, p<0.001). Gender, age, body weight, body mass index, total protein, albumin, red cell count, hemoglobin, hematocrit, platelet, vitamin B12, and triglyceride levels were unrelated to low VE levels.

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Among the 55 patients, 7 (12.7%) had peripheral neuropathy. Sensory polyneuropathy developed in 7 (58.3%) of the 12 patients in the low VE group and was characterized by glove-and-stocking type of superficial sensory loss and decreased deep tendon reflexes. All patients with sensory polyneuropathy responded to treatment with oral VE. On multivariate analyses, the white cell count and total cholesterol level were associated with low VE levels. The total cholesterol level was the most salient contributing factor. Decreased VE levels ascribed to VE malabsorption after gastrectomy for gastric cancer were observed in approximately 15% of patients, some of whom also had sensory polyneuropathy. Patients with a low serum level of VE, a fat-soluble vitamin, tended to have significantly decreased levels of total cholesterol, which may be attributed to vitamin E malabsorption as well as fat malabsorption. In patients with neurologic symptoms and low serum total cholesterol levels that do not respond to treatment with vitamin B12, hypovitaminosis E should be suspected.

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