

B12

A Study for Incidence and Treatment of Vitamin B12 Deficiency after Total Gastrectomy

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Purpose: Vitamin B12 (VB12) deficiency is an inevitable sequela of a total gastrectomy, which results in general symptoms, including easy fatigue, and hematological, neurological, and gastrointestinal complications. Especially in cases of neurological injury, it may be irreversible if the timely treatment is delayed. Therefore the early diagnosis and treatment is essential. However, no guidelines exist for the incidence or treatments.

Methods: We investigated the symptoms and serum VB12 concentrations of 296 patients who underwent a total gastrectomy for a gastric malignancy. We defined 200-300 pg/ml as the mild decrease group, under 200 pg/ml as the severe decrease group, and over 300 pg/ml as the normal limit.

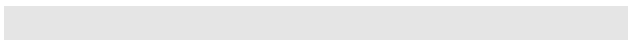
Results: The cumulative incidence of VB12 deficiency were 5.1, 11.2, 29.9, 44.7, 64.5% at 6 month, 1, 2 and 3 years, and at 4 or more years, respectively. The 90% of patients reported at least 1 symptom. The group under 200 pg/ml was supplemented at 1 month intervals; 10 of the 16 patients (63%) had their VB12 elevated to above 300 pg/ml. The group between 200-300 pg/ml was supplemented at 1 or 3 month intervals; 21 out of 23 (91%), and 12 out of 15 patients (80%) had their B12 elevated to above 300 pg/ml at the 1 and 3 month intervals, respectively, but with no statistical significance.

Conclusion: The group with a V12 under 200 pg/ml should be supplemented 6 times, at 1 month intervals, regardless of the symptom presentation, and when the rechecked serum VB12 level has been increased above 300 pg/ml, it should be supplemented at 3 month intervals. In the group with a VB12 between 200 and 300 pg/ml, the VB12 should

be supplemented at 3 month intervals if the symptom is present, and the asymptomatic group should be observed. (J Korean Surg Soc 2003;64:206-211)

Key Words: Total gastrectomy, Vitamin B12 deficiency, Vitamin B12 supplementation
: B12

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가 가
가 .(1,2)
가 가 가
50% .(3,4)
B12 .(1,5-7)
50% 1
B12
가 B12
B12

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B12

1992 6 2001 12

296
732

58.7 , 62.1 .
가 187 , 가 109
가 477 , 가 255

Roux-en-Y -
Billroth II

B12 6 6
200 pg/ml , 200~300 pg/ml , 300
가

B12 Actinamide 1,000 µg 1

가 1 3

B12 가 B12

1) B12

B12 58
() 511(196~2293) pg/ml .
B12 가 300
pg/ml

6 15 /296 (5.1%), 1 27 /241 (11.2%),
2 55 /164 (29.9%), 3 55 /123 (44.7%), 4
60 /93 (64.5%) (Fig. 1). 200 pg/ml
60 16 .
6 9 /732 (1.2%), 1
16 /660 (2.4%), 2 27 /527 (5.1%), 3
31 /434 (7.1%), 4 35 /359 (9.7%), 5
52 /300 (17.3%) (Fig. 2). 52
200 pg/ml 5 .

2) B12 B12

가 60
54 6
33 (55%) ,
31 (52%) , 25
(42%) , 14
(23%) B12가
52 10 ,
가 (32 ,
62%), (22 , 42%), (13 , 25%)
(Table 1).

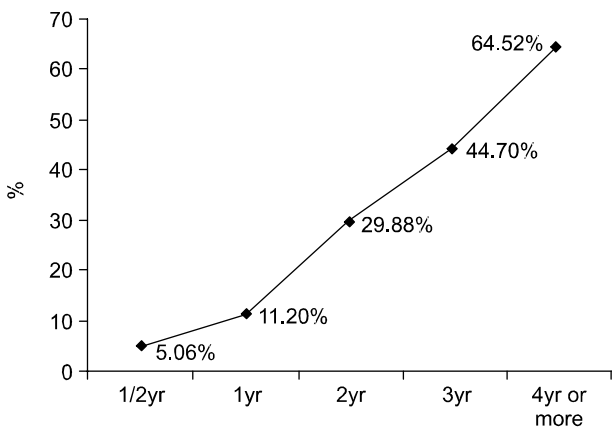


Fig. 1. Cumulative incidence of vitamin B12 deficiency after total gastrectomy.

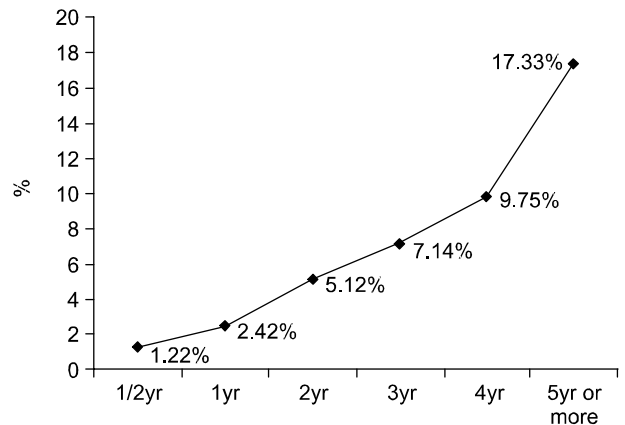


Fig. 2. Cumulative incidence of vitamin B12 deficiency after subtotal gastrectomy.

Table 1. Incidence of symptoms related with vitamin B12 levels after gastrectomy

	Vit B12 levels after TG		Vit B12 levels after STG	
	< 200 pg/ml n=16 (%)	200~300 pg/ml n=44 (%)	< 200 pg/ml n=5 (%)	200~300 pg/ml n=47 (%)
Fatigue	3 (18.8)	17 (38.6)	2 (40.0)	21 (44.7)
Dizziness	5 (31.3)	12 (27.3)	4 (80.0)	14 (29.8)
Anorexia	1 (6.3)	1 (2.3)	0 (0.0)	5 (10.6)
Dyspepsia	2 (12.5)	3 (6.8)	0 (0.0)	5 (10.6)
Diarrhea	3 (18.8)	3 (6.8)	0 (0.0)	10 (21.3)
Glossitis	2 (12.5)	3 (6.8)	1 (20.0)	0 (0.0)
PPN	6 (37.5)	10 (22.7)	1 (20.0)	13 (27.7)
Impotence	0 (0.0)	4 (9.1)	1 (20.0)	2 (4.3)
Loss of taste	0 (0.0)	1 (2.30)	0 (0.0)	1 (2.1)
Incoordination	0 (0.0)	3 (6.8)	0 (0.0)	0 (0.0)
Memory loss	4 (0.0)	10 (22.7)	1 (20.0)	8 (17.0)
Loss of vib. sense	0 (0.0)	2 (4.5)	0 (0.0)	1 (2.1)
Hair loss	2 (12.5)	1 (2.3)	0 (0.0)	1 (2.1)
C.leucoplakia	1 (6.3)	1 (2.3)	0 (0.0)	0 (0.0)
M.weakness	1 (6.3)	7 (15.9)	0 (0.0)	5 (10.6)
Irritability	2 (12.5)	6 (13.6)	0 (0.0)	4 (8.5)
M.anemia	6 (37.5)	19 (43.2)	0 (0.0)	13 (27.7)
Atrophy	0 (0.0)	3 (6.8)	0 (0.0)	0 (0.0)
No Sx	1 (6.3)	5 (11.4)	0 (0.0)	10 (21.3)

TG = total gastrectomy; STG = subtotal gastrectomy; PPN = peripheral neuropathy; Vib. sense = vibration sense; C.leucoplakia = cervical leucoplakia; M.weakness = muscle weakness; M.anemia = macrocytic anemia.

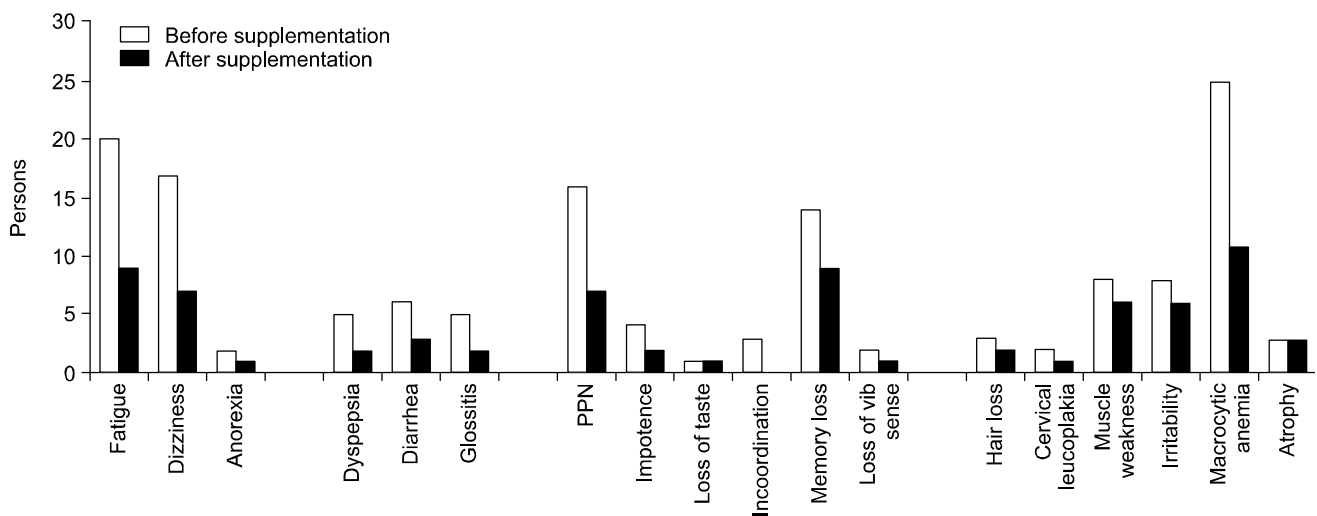
**Fig. 3.** Incidence of symptoms before and after vitamin B12 supplementation.

Table 2. Treatment results according to the interval of vitamin B12 supplementation

	1 month interval (n=39)	3 month interval (n=15)
Serum conc.(pg/ml)		
Pre-treat (mean)	197.7	245.9
Post-treat (mean)	503.6	382.0
No. of supplementation	5.7	3.8
No. of cases below 300 pg/ml after treatment	8.0	3.0

Table 3. Comparison of treatment results according to the interval of vitamin B12 supplementation in the group of serum conc. 200~300 pg/ml

	1 month interval (n=39)	3 month interval (n=15)
Serum conc. (pg/ml)		
Pre-treat (mean)	225.5	245.9
Post-treat (mean)	576.7	382.0
No. of supplementation	4.3	3.8
No. of cases below 300 pg/ml after treatment*	2.0	3.0

*Fischer-exact test; P>0.05

B12 (Fig. 3), 56.4% (22/39), 56.3% (9/16), 56% (14/25), 54, 11 (20.4%), 가 300 pg/ml 가 3 60.9% (28/46), 44.4% (12/27), 87.5% (14/16), 23.1% (3/13)

200~300 pg/ml 1 43 1 23 20 3 1 4.3 가 23 21 (91%) 300 pg/ml 가 3 3.8 20 가 15 12 (80%) 300 pg/ml 가 (Table 3). 가 200~300 pg/ml Fischer-exact test P>0.05

3)

가 60 1 , 39 1 5.7 B12 가 197.7 (107~207) pg/ml 503.6 (162~2100) pg/ml 가 , 293.6 (0~1885) pg/ml 39 8 1 6 가 300 pg/ml , 200 pg/ml (162 pg/ml) 1 7 가 3 2.5 5 300 pg/ml 가 60 20 3 , 3.8 가 15 가 245.9 pg/ml 382 pg/ml 가 15 3 2 300 pg/ml 2 가 6 , 3 1 300 pg/ml 가 (Table 2). 가 200 pg/ml 200~300 pg/ml 16 1 , 6.6 (3~10) 10 (62.5%) 300 pg/ml 가 6 (37.5%) 300 pg/ml

B12 B12 R-binder R-binder (Intrinsic factor) (8,9) B12 DNA 가 1 5 (10,11) Sumner (12) 31% B12 , Shinya (13)

23% , (glossitis) .
 64.5% 4 , ,
 9 17.3% Alzheimer's disease
 (>200 pg/ml) 가
 (300 pg/ml) . (21,22)
 4 B12 B12
 (I)
 (intrinsic factor) B12 가 가
 B12 가 가 B12 가 200~300 pg/ml
 .(12,14, 가
 15) Okuda (16) Shinya (13) B12 가
 가 200 pg/ml
 B12 가 200~300 pg/ml P-value
 가 P>0.05
 B12 가 가 200~300 pg/ml
 가 200 pg/ml 가
 B12 . B12
 .(17) Sumner (12) 200~300 pg/ml
 B12 .
 32% , 가 200 pg/ml
 42% , B12 가 25% 1 16 가 10 (62.5%)
 B12 가 가 300 pg/ml ,
 가 200 pg/ml 6 3
 5
 가 200~300 pg/ml 1
 3 1
 가 23 21 (91.3%) , 3
 .(3,12,18) 15 12 (80%)
 ,(17) 가 300 pg/ml 가 Fischer-exact
 B12 MCV(mean test P > 0.05
 corpuscular volume) 가 1 3
 ,(19) B12 가 가
 1 3
 가
 (12,14,15) 가 Kapadia (20)
 B12 가 200~300 pg/ml
 가 B12
 B12 가
 homocysteine methylmalonic acid
 가 200 pg/ml
 B12
 B12

가

B12

Shinya (13) 가

B12 가

가

1 3

60

(60 /60)가

6 B12

B12 가 200 pg/ml

1 1 1000µg

Actinamide 6 3 가 200~300

pg/ml 3

pg/ml 200 ~ 300

200 pg/ml

B12

and jejunal morphology after total gastrectomy for carcinoma of the stomach. *Surg Gynecol Obstet* 1986;163:225-30.

6) Bradley III EL, Issacs J, Hersh T, Davidson ED, Millikan W. Nutritional consequences of total gastrectomy. *Annals of Surgery* 1975;182:415-29.

7) Armbrecht U, Lundell L, Lindstedt G, Stockbruegger RW. Causes of malabsorption after total gastrectomy with Roux-en-Y reconstruction. *Acta Chir Scand* 1988;154:37-41.

8) Clementz GL, Schade SG. The spectrum of vitamin B12 deficiency. *Am Fam Physician* 1990;41:150-62.

9) Babior BM. Megaloblastic anemias. In: Anthony SF, Eugene B, editors. *Harrison's Principles of internal medicine*. 14th ed. New York: Mcgraw-Hill companies; 1998. p.653-6.

10) Moreno AH. Studies on nutritional and other disturbances following operations for cancer of the stomach. *Ann Surgery* 1956;144:779-808.

11) Keith BT, Luean EA. Cobalamin in nutrition: Clinical nutrition. 2nd ed; 1983. p.319-25.

12) Sumner AE, Chin MM, Abrahm JL, Berry GT, Gracely EJ, Allen RH, et al. Elevated methylmalonic acid and total homocysteine levels show high prevalence of vitamin B12 deficiency after gastric surgery. *Ann Intern Med* 1996;124:469-76.

13) Adachi S, Kawamoto T, Otsuka M, Todoroki T, Fukao K, et al. Enteral vitamin B12 supplements reverse postgastrectomy B12 deficiency. *Annals of Surgery* 2000;232:199-201.

14) Leeming RJ. Cobalamin and folate deficiencies. *Clin Lab Haematol* 1996;18:126-7.

15) Norman EJ. Urinary methylmalonic acid/creatinine ratio: a gold standard test for tissue vitamin B12 deficiency. *J Am Geriatr Soc* 1999;47:1158-9.

16) Okuda K. Discovery of vitamin B12 in the liver and its absorption factor in the stomach. *J Gastroenterol Hepatol* 1999;14:301-8.

17) Stabler SP. Vitamin B12 deficiency in older people: improving diagnosis a preventing disability. *J Am Geriatr Soc* 1998;46:1317-9.

18) Klipstein FA. Iron and vitamin B12 deficiency following subtotal gastrectomy. Report of a patient developing polycythemia vera following treatment. *Ann Intern Med* 1962;57:133-40.

19) Smith TJ, Malon RG. Vitamin B12 deficiency and early rise in mean corpuscular volume. *JAMA* 1982;247:1126.

20) Kapadia CR. Vitamin B12 deficiency after gastric surgery: its early detection. *Gastroenterology* 1996;111:1151-2.

21) Harju E. Metabolic problems after gastric surgery. *Int Surgery* 1990;75:27-35.

22) Heaton EB, Savage DG, Brust JC, Garrett TJ, Lindenbaum PJ. Neurologic aspects of cobalamin deficiency. *Medicine (Baltimore)* 1991;70:229-45.

REFERENCES

1) Bae JM, Park JW, Yang HK, Kim JB. Nutritional status of gastric cancer patients after total gastrectomy. *World J Surg* 1998;22:254-61.

2) Korea national statistical office. Annual report on the cause of death statistics. Gwacheon, Ministry; 2001.

3) Bradley III EL, Issacs J. Postresectional anemia. *Arch Surgery* 1976;111:844-8.

4) Adams JF. The clinical and metabolic consequences of total gastrectomy: II. Anemia: Metabolism of iron, vitamin B12 and folic acid. *Scand J Gastroenterol* 1968;3:145-51.

5) Cristallo M, Braga M, Agape D, Primignani M, Zuliani W, Vecchi M, et al. Nutritional status, functional small intestine