Note

Gastric and Jejunal Enteral Feeding Differently Affect Vitamin B₁₂ Status in Subjects with Severe Motor and Intellectual Disabilities

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Summary The absorption of vitamin B₁₂ is a complex process involving gastric acid and intrinsic factor as the indispensable components. In this study, we have investigated the effects of the administration site in enteral feeding on vitamin B₁₂ status in subjects with severe motor and intellectual disabilities (SMID). This is a cross-sectional study conducted from January to June 2016. Blood concentrations of vitamin B₁₂, folate, vitamin B₆, and homocysteine (Hcy) were measured in a total of 82 subjects (38 men, 44 women). Also, nutrients intake was assessed. Subjects with enteral feeding (EF) had significantly higher intakes of vitamin B₁₂, folate, and vitamin B₆ than those with oral ingestion (OI). Serum folate and vitamin B₆ concentrations in subjects with EF were significantly higher than those with OI. Among the EF subjects, serum vitamin B₁₂ concentration was significantly higher in those fed with gastric tube than those fed with jejunal tube in spite of similar vitamin B₁₂ intakes. No significant difference was observed between the two groups regarding the circulating concentrations of folate, vitamin B₆, or Hcy. Although each administration route has its own benefit, gastric tube is advantageous in the absorption of vitamin B₁₂.

Key Words vitamin B₁₂, enteral feeding, stomach, jejunum, severe motor intellectual disabilities

Vitamin B₁₂ is absorbed by a unique system. After its release from foods by the action of gastric acid, vitamin B₁₂ binds to intrinsic factor (IF) secreted from the gastric parietal cells. Then, vitamin B₁₂-IF complex is specifically absorbed from the distal ileum (1). Thus, stomach plays crucial roles in the absorption of vitamin B₁₂, which is illustrated by various clinical observations; e.g., anemia due to vitamin B₁₂ deficiency in such conditions as post-gastrectomy and gastric mucosal atrophy due to autoimmunity against gastric parietal cells (1, 2).

Enteral or parenteral feeding is employed in subjects incapable of oral intake. Of these, enteral feeding is preferred as far as their gastrointestinal tract is intact and usable for feeding, since it has various beneficial properties compared with parenteral feeding such as less susceptibility to infection, less likelihood to mucosal atrophy and resultant bacterial translocation (3, 4).

In the enteral nutrition, feeding tube can be placed either in the stomach or jejunum (5). Considering the critical roles of stomach in the absorption of vitamin B₁₂, it was considered likely that the absorbing capacity

for vitamin B₁₂ and vitamin B₁₂ status would be greatly affected by where the feeding tube is placed, for which, however, no previous articles were found as far as we have searched.

Then, in this paper, we have studied the vitamin B₁₂ status in subjects with severe motor and intellectual disabilities (SMID) who were enterally fed via gastric or jejunal tube. Subjects with SMID were selected as the study model, since a substantial percentage of them are enterally fed, but mostly free from gastrointestinal dysfunction (6).

Subjects and Methods

This is a cross-sectional study conducted from January to June in 2016. The study subjects were those with SMID living in the residential hospital, the Biwakogakuen Kusatsu Medical and Welfare Center for Disabilities. Written consent to participate in this study was obtained from each subject or proxy after explanation of the objective and protocol of this study. The study protocol was approved by the Ethical Committee of the residential hospital, the Biwakogakuen Kusatsu Medical and Welfare Center for Disabilities (Ethics Approval

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Table 1. Characteristics of subjects.

	Total (n=82)	Men (n=38)	Women (n=44)	<i>p</i> value
Age (y)	46.1±12.3	46.8±13.7	45.5±11.2	0.653
Height (cm)	148.0±10.9	151.7±9.9	144.8±10.9	0.004
Weight (kg)	37.8±8.1	38.1±6.9	37.5±9.1	0.730
BMI (m ² /kg)	17.3±3.6	16.6±2.9	17.9±4.0	0.098
Serum albumin (g/dL)	3.9±0.4	4.0±0.3	3.9±0.5	0.362
Serum total cholesterol (mg/dL)	180.8±29.8	171.2±27.4	189.1±29.6	0.006
Blood hemoglobin (g/dL)	13.6±1.5	13.7±1.5	13.5±1.4	0.530
Serum creatinine (mg/dL)	0.40±0.17	0.43±0.17	0.38±0.16	0.155
eGFR _{cys} (mL/min/1.73 m ²)	101.2±24.8	96.5±22.0	105.3±26.6	0.112
Serum vitamin B ₁₂ (pmol/L)	596.7±220.1	587.1±217.3	604.9±224.6	0.717
Serum folate (nmol/L) ¹	35.9 (14.9, 45.3)	36.1 (15.3, 45.3)	34.3 (14.6, 45.3)	0.989
Serum vitamin B ₆ (pmol/mL) ¹	76.6 (60.2, 105.3)	78.2 (57.5, 106.5)	76.3 (62.2, 106.1)	0.882
Plasma Hcy (μmol/L)	8.8±4.4	9.5±3.8	8.2±4.9	0.192

Data are expressed as mean±SD, and comparison was made using Student's *t* test unless otherwise indicated.

¹Data are expressed as median (Q1, Q3), and comparison was made using Mann Whitney's *U* test.

number; 2015101), and the study was done complying with the Declaration of Helsinki. The exclusion criteria were treatment with vitamin B₁₂, folate or vitamin B₆. Those aged less than 18 y old were also excluded. A total of 82 subjects (38 men, 44 women) were included in the analysis.

Non-fasting blood was drawn by venipuncture between breakfast and lunch. After centrifugation, serum or plasma was stored at −30°C until measurement. Serum concentrations of vitamin B₁₂ and folate were measured by chemiluminescent enzyme immunoassay (CLEIA). Serum vitamin B₆ and plasma homocysteine (Hcy) concentration were measured by HPLC (7, 8). Serum concentrations of albumin and total cholesterol were measured by dye-binding methods using bromocresol green (BCG) and enzymatic method using cholesterol oxidase, respectively. Their renal function was evaluated by cystatin C-based estimated glomerular filtration rate (eGFR; mL/min/1.73 m²) which was calculated as $(104 \times \text{cystatin C}^{-1.019} \times 0.996^{\text{age}}) - 8$ for men and $(104 \times \text{cystatin C}^{-1.019} \times 0.996^{\text{age}} \times 0.929) - 8$ for women (9).

Dietary intake was calculated according to the dietary record method by one of the authors (MK, registered dietitian), and results from 7 d were averaged. Subjects with oral intake (OI) took their meals three times a day; at 7 am, 11:30 am, and 5 pm. CZ-Hi™, San Etto™ and Recovery New Treat™ were the formulas mainly used for enteral feeding (EF). Subjects with EF were given these formulas three or four times a day; at 5 am, 11 am, 4 pm, and 8 pm. In most subjects with EF, 200–400 kcal was injected at one time and the duration was 1 h for gastric tube and 3 to 4 h for jejunal tube. In this study, serum total vitamin B₁₂ concentration was measured as a parameter for vitamin B₁₂ nutritional status, which reflects vitamin B₁₂ intake and its bodily store. It is a useful indicator for long-term status, and little affected by the interval between the meal and veni-

puncture, or the difference in the duration of injection time (10). The number of subjects with OI, EF, and both was 36, 39, and 7, respectively. Statistical analyses were done using SPSS version 22 (IBM Japan, Tokyo). The difference between two independent groups was analyzed by Student's *t* test. Mann Whitney's *U* test was employed for serum folate and vitamin B₆ concentrations, since serum folate concentration exceeded the upper detection limit of 45.3 nmol/L in some subjects, and serum vitamin B₆ concentration was not normally distributed. In the analysis comparing the effects of subjects' injection site, those with both OI and EF were excluded. The significance level of the associations was set at *p*<0.05.

Results

Table 1 shows the baseline characteristics of the 82 subjects (38 men, 44 women) included in the analysis. They were aged 46.1 y as the average with their mean BMI being 17.3 kg/m². Of note, their mean serum creatinine was as low as 0.40 mg/dL, which is likely to reflecting their extremely low skeletal muscle volume. Although renal function is usually evaluated by creatinine-based eGFR, we have employed cystatin C-based eGFR in this study, since creatinine-based eGFR would over-estimate the renal function in subjects with extremely decreased muscle mass. Their serum vitamin B₁₂, folate, and vitamin B₆ concentrations were not in the range of deficiency (11, 12).

The intakes of protein, fat, and carbohydrates were higher in subjects with OI than those with EF. On the contrary, the intakes of vitamin B₁₂, folate, and vitamin B₆ were higher in subjects with EF than those with OI (Table 2). In addition, serum folate and vitamin B₆ concentrations were significantly higher in subjects with EF than those with OI. Serum vitamin B₁₂ concentration was higher in subjects with EF than those in OI, although not statistically significant. In addition, plasma Hcy concentration was significantly lower in

Table 2. Comparison of nutrients intake, vitamins and Hcy status based on the type of feeding.

	Oral intake (n=36)	Enteral feeding (n=39)	p value
Age (y)	50.5±11.0	42.3±12.5	0.003
Height (cm)	148.2±10.1	147.6±11.8	0.890
Weight (kg)	35.6±7.5	39.5±8.8	0.046
BMI (m ² /kg)	16.3±3.2	18.2±3.9	0.023
Serum albumin (g/dL)	4.1±0.3	3.8±0.4	<0.001
Serum total cholesterol (mg/dL)	189.1±30.3	174.3±29.2	0.035
Blood hemoglobin (g/dL)	13.3±1.3	14.0±1.6	0.065
Serum creatinine (mg/dL)	0.48±0.18	0.33±0.13	<0.001
eGFRcys (mL/min/1.73 m ²)	101.9±24.9	100.0±26.1	0.743
Serum vitamin B ₁₂ (pmol/mL)	537.0±165.1	626.5±254.2	0.073
Serum folate (nmol/mL) ¹	14.6 (9.5, 20.5)	44.6 (39.2, 45.3)	<0.001
Serum vitamin B ₆ (pmol/mL) ¹	68.1 (55.2, 79.0)	86.5 (70.6, 117.4)	0.013
Plasma Hcy (μmol/L)	10.2±3.9	7.8±4.9	0.025
Energy intake (kcal/d)	1399±240	951±154	<0.001
Protein (g/d)	54.4±9.3	44.8±9.6	<0.001
(%E/d)	(15.6±1.1)	(19.0±3.0)	<0.001
Fat intake (g/d)	43.0±8.9	23.9±7.6	<0.001
(%E/d)	(27.7±3.0)	(22.4±5.9)	<0.001
Carbohydrates intake (g/d)	190.1±35.0	146.9±27.4	<0.001
(%E/d)	(54.3±3.1)	(62.0±7.0)	<0.001
Vitamin B ₁₂ (μg/d)	3.0±0.7	4.2±2.3	0.005
Folate (μg/d)	210.1±39.5	298.8±109.1	<0.001
Vitamin B ₆ (mg/d)	0.9±0.3	2.6±1.0	<0.001

Data are expressed as mean±SD, and comparison was made using Student's *t* test unless otherwise indicated.

¹ Data are expressed as median (Q1, Q3), and comparison was made using Mann Whitney's *U* test.

Table 3. Comparison of vitamins and Hcy status based on the injection site in enteral feeding.

	Stomach (n=22)	Jejunum (n=17)	p value
Age (y)	43.3±13.9	41.0±10.7	0.580
Height (cm)	148.6±12.4	146.3±11.3	0.524
Weight (kg)	40.1±8.0	38.6±9.9	0.610
BMI (m ² /kg)	18.2±3.6	18.1±4.4	0.933
Serum albumin (g/dL)	3.8±0.4	3.7±0.4	0.202
Serum total cholesterol (mg/dL)	179.5±32.2	167.7±24.2	0.217
Blood hemoglobin (g/dL)	14.2±1.3	13.7±1.8	0.335
Serum creatinine (mg/dL)	0.33±0.14	0.33±0.12	0.961
eGFRcys (mL/min/1.73 m ²)	102.5±28.6	96.7±22.9	0.503
Serum vitamin B ₁₂ (pmol/mL)	732.9±237.8	488.8±208.8	0.002
Serum folate (nmol/mL) ¹	43.5 (36.0, 45.3)	45.3 (40.3, 45.3)	0.362
Serum vitamin B ₆ (pmol/mL) ¹	86.6 (57.5, 109.6)	80.5 (71.0, 133.6)	0.726
Plasma Hcy (μmol/L)	7.1±1.7	8.8±7.1	0.340
Vitamin B ₁₂ intake (μg/d)	4.0±1.6	4.4±3.1	0.647
Folate intake (μg/d)	283.6±67.8	318.5±146.7	0.329
Vitamin B ₆ intake (mg/d)	2.6±0.8	2.6±1.2	0.846

Data are expressed as mean±SD, and comparison was made using Student's *t* test unless otherwise indicated.

¹ Data are expressed as median (Q1, Q3), and comparison was made using Mann Whitney's *U* test.

subjects with EF than those in OI (Table 2).

In subjects under EF, serum vitamin B₁₂ concentration was significantly higher in those fed with gastric tube than those fed with jejunal tube, whereas circulating concentrations of folate, vitamin B₆, or Hcy were no

different between the two groups (Table 3).

Discussion

The implication of this paper is twofold, one related to the nutritional assessment of SMID subjects, and the

other regarding the effect of gastric and jejunal feeding on vitamin B₁₂ status. First, subjects with SMID have various health problems including nutritional ones. However, reports on the vitamin status in subjects with SMID have been quite limited, except for the effect of anti-epileptic drugs, which are commonly administered to people with SMID, on the catabolism of vitamin D and folate deficiency (13, 14). Studies on water-soluble vitamins including vitamin B₁₂ have been scarce. However, vitamin B₁₂ deficiency is well known to cause megaloblastic anemia, and also to be a risk for various diseases such as vascular disorder, osteoporotic fracture, and impaired physical function due to hyperhomocysteinemia (15). Therefore, we have considered it worthwhile to study the vitamin B₁₂ status in SMID.

In subjects with EF, serum concentrations of folate and vitamin B₆ were higher and plasma Hcy level was lower than those with OI, probably reflecting the higher intake of these vitamins in those with EF.

EF through jejunal route is advantageous over gastric route in that it is less likely to cause gastroesophageal regurgitation and aspiration pneumonitis (16, 17). Thus, jejunal route is often preferred as long as it can be safely performed. However, the effect of administration route on vitamins availability has not been reported as far as we have searched. Our results have revealed the beneficial effect of gastric route for vitamin B₁₂ status, and suggest that the possible impairment of vitamin B₁₂ absorption should be taken into account in EF via jejunal route.

Disclosure of state of COI

The authors declared no conflict of interest.

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