

Serum Vitamin B₁₂, Folic Acid, Ferritin and Hematologic Status in Patients with Bladder Substitution

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ABSTRACT

Vitamin B₁₂ below reference level was found in 12.5% of the patients who underwent bladder substitution by ileal conduit (IC) surgical technique and in 10% of the patients using Mainz pouch (MP) technique. Anemia was found in 31.3% of the IC group and in 20% of the MP group but none of the patients developed iron-deficiency anemia. Serum folic acid was within the reference range in all patients. The mean levels of all biochemical and hematologic parameters in both groups were not significantly different. With regard to the follow up period, the number of patients with vitamin B₁₂ deficiency was higher in the group with the follow-up period of more than 5 years compared to that with the follow-up period of less than 5 years (18.2% vs 6.7%).

Key words: Vitamin B₁₂, Folic acid, Anemia, Bladder substitution, Ileal conduit, Mainz Pouch

INTRODUCTION

The use of an intestinal portion, particularly the small intestine for bladder substitution may alter the absorption process and can result in nutritional deficiencies. It is known that the ileum is the absorption site for vitamin B₁₂. Thus the removal of these segments has the potential to increase the risk of vitamin B₁₂ deficiency. Vitamin B₁₂ can not be synthesized in human and must be obtained from animal products which is the main dietary source. Free vitamin B₁₂ must be released from dietary protein and bound to an intrinsic factor in the stomach. The vitamin B₁₂ intrinsic factor complex moves to the ileum and is attached to a specific membrane receptor of the ileum and is then absorbed by endocytosis (Seetharam et al., 1981). The objective of this study was to assess the level of vitamin B₁₂, folic acid and hematologic status in patients from whom part of the terminal ileum had been removed for urological reconstruction.

MATERIALS AND METHODS

Patients

A total of 26 patients with invasive bladder cancer who underwent bladder replacement at Maharaj Nakorn Chiangmai Hospital, Chiang Mai, Thailand between 1983-1999 were recruited. They consisted of 22 men and 4 women with a mean age of 61 years (range 37 to

83). The mean post operative follow up period was 59 months (range 9 to 179). Two different techniques of bladder substitution were used. Sixteen patients were operated with the ileal conduit (IC) technique whereas ten patients underwent Mainz pouch (MP) reconstruction.

Surgical techniques

In the case of ileal conduit replacement, we used a stretch of 15 cm of the distal ileum, 10 cm distal from the ileocecal valve, to create the incontinence diversion and for the Mainz pouch, we used a piece of 20 - 30 cm of the terminal ileum and 15 cm of the ascending colon including the ileocecal valve to create the neobladder.

Chemical analysis

Eight ml of venous blood sample was taken for measurement of hemoglobin, hematocrit, serum ferritin, serum vitamin B₁₂ and folic acid concentration. Hemoglobin was measured immediately on a specimen collected in EDTA – containing tubes by using fully automatic blood cell electronic counter (Coulter Model STKS, Coulter Corporation, Miami, Florida, USA). Hematocrit was measured by centrifuging a heparin-containing capillary tube at 2000 x g for 5 minutes at room temperature and comparing the height of the column of packed cells with the height of the entire column of red blood cell and plasma. The remaining of the blood sample was collected in a vacuum tube containing no anticoagulant. Within one hour, the sample was centrifuged at 3,000 revolutions per minute for 10 minutes and the separated serum was divided into aliquots that were stored at - 20 °C prior to analysis. Serum ferritin was measured by an enzyme-linked immuno sorbent assay (ELISA), employing horse radish peroxidase as an enzyme label and microtitre plate as solid phase (Linpisarn et al., 1981). Serum vitamin B₁₂ and folic acid concentration were determined, using a simultaneous radioassay kit (Dual Count Solid Phase No Boil Assay, KDSP1, Diagnostic Products Corporation, Los Angeles, CA, USA.), and read by a gamma counter (D 501001 Model 5010 COBRA QUANTUM, Automatic Gamma Counter, Packard Instrument Company, CT, USA.).

A hemoglobin value below 12 g/dl and a hematocrit below 36% were regarded as indications of iron deficiency anemia. Serum ferritin level of less than 15 ng/ml was considered as iron depletion (Cook and Finch, 1979). The normal reference range of serum vitamin B₁₂ and serum folic acid, based on the company's leaflet were 200 - 950 pg/ml and 3.0 – 17.0 ng/ml respectively.

Statistical analysis

Comparison between two groups was done using Student's t test. All data were presented as mean±SD unless otherwise stated and a P<0.05 value was considered significant.

RESULTS

Post operative measurement of hemoglobin, hematocrit, vitamin B₁₂, ferritin and folic acid in both groups revealed no significant difference. In the IC group, anemia was found in 31.3% of the patients in contrast to 20% in the MP group. Iron depletion occurred only in the IC group (6.3% of the cases) but none of the patients developed iron-deficiency anemia.

Vitamin B₁₂ deficiency was found in 12.5% and 10% of the IC and MP group respectively. Folic acid concentration was within the normal range in all patients. The mean levels of all biochemical and hematologic parameters were compared in both groups and showed no statistical difference (Table 1). Regarding to the follow up period, it was found that the number of patients with vitamin B₁₂ deficiency increased with time from 6.7% in the less than five year follow-up group to 18.2% in the more than five year follow-up group (Table 2).

Table 1. Comparison of serum vitamin B₁₂, folic acid, ferritin and hematologic status in patients with ileal conduit and Mainz pouch surgical technique.

| | Ileal conduit (16)* | Mainz pouch (10)* | |
|-----------------------------------|------------------------|----------------------|-------------|
| | Mean±SD | Mean±SD | p value |
| Age (year) | 61.2 ± 11.2 | 60.8 ± 8.6 | 0.91 |
| Hb (g%) | 12.41 ± 1.36 | 13.33 ± 1.63 | 0.13 |
| < 12 | (5/16 = 31.3%) | (2/10 = 20%) | |
| Hct (%) | 37.8 ± 4.1 | 39.7 ± 5.06 | 0.29 |
| < 36 | (3/16 = 18.8%) | (2/10 = 20%) | |
| Vit B₁₂ (pg/ml) | 512.1 ± 268.5 | 515.0 ± 328.9 | 0.98 |
| < 200 | (2/16 = 12.5%) | (1/10 = 10%) | |
| Ferritin (ng/ml) | 164.9 ± 141.8 | 97.4 ± 45.8 | 0.16 |
| < 15 | (1/16 = 6.3%) | none | |
| Folic acid (ng/ml) | 9.0 ± 3.4 | 7.8 ± 5.9 | 0.51 |
| < 3.0 | none | none | |

*number of patients

Table 2. Comparison of the serum vitamin B₁₂, folic acid, ferritin and hematologic status in patients with a follow-up period of less and greater than five years for both surgical techniques.

| | Follow up < 5 years (15)* | Follow up > 5 years (11)* | p value |
|-----------------------------------|------------------------------|------------------------------|-------------|
| Hb (g/dl) | 12.44 ± 1.40 | 13.20 ± 1.61 | 0.21 |
| < 12 | (4/15 = 26.7%) | (3/11 = 27.3%) | |
| Hct (%) | 37.8 ± 4.2 | 39.5 ± 4.9 | 0.36 |
| < 36 | (3/15 = 20%) | (2/11 = 18.12%) | |
| Vit B₁₂ (pg/ml) | 513.3 ± 244.8 | 513.1 ± 348.8 | 1.0 |
| < 200 | (1/15 = 6.7%) | (2/11 = 18.2%) | |
| Ferritin (ng/ml) | 158.2 ± 145.2 | 112.6 ± 63.3 | 0.34 |
| < 15 | (1/15 = 6.7%) | none | |
| Folic acid (ng/ml) | 8.8 ± 3.7 | 8.1 ± 5.5 | 0.71 |
| < 3.0 | none | none | |
| Age (year) | 61.1 ± 11.1 | 61.1 ± 9.1 | 1.0 |

*number of patients

DISCUSSION AND CONCLUSION

The use of a bowel segment for construction of the urinary tract is increasing nowadays and this may result in malabsorption of some nutrients from the intestine. In a previous study (Thompson et al., 1972), it appeared that resection of 45 cm or more of the ileum was likely to result in either vitamin B₁₂ or fat malabsorption. Since human are not able to synthesize vitamin B₁₂, it must be ingested as food. It is absorbed in the terminal ileum by a gastric intrinsic factor and is mostly deposited in the liver and bone marrow. Complete vitamin B₁₂ deficiency may manifest after 3 to 6 years but partial vitamin malabsorption may become clinically evident only as long as after 30 years (Herbert and Colman, 1988). Malabsorption of vitamin B₁₂ can result in megaloblastic anemia, Hunter's glossitis and/or a spinocerebellar degenerative disease. However, vitamin B₁₂ deficiency may also remain completely asymptomatic. In our study, two patients in the IC group and one in the MP group with serum vitamin B₁₂ levels below normal range remained asymptomatic.

The degree of disturbed absorption may depend on the length of the ileal segment removed. Some studies demonstrated that a resection of more than 60 cm of the terminal ileum caused malabsorption of bile acid and vitamin B₁₂. No disturbances were noted when less than 60 cm of the ileum were resected (Thompson and Wrathell, 1977; Filipsson et al., 1978). In this study, we observed no difference in the absorption ability of vitamin B₁₂ and folic acid between the two surgical techniques employed. Several studies reported that approximately 5 to 8% of the elderly in Caucasian population showed vitamin B₁₂ values below reference range (McRae and Freedman, 1989; Bunting et al., 1990). In this study, although approximately 70% of the patients were older than 60 years, we found that 11.5% of the patients developed vitamin B₁₂ deficiency. Therefore, it was likely that vitamin B₁₂ deficiency of these patients might be due to long term effects of urinary diversion. Folic acid can be absorbed by the entire small intestine (Racioppi et al., 1997), thus none of the patients developed serum folic acid level below the normal range.

In conclusion, serum vitamin B₁₂ level in patients with bladder substitution by using terminal ileum should be monitored regularly.

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