Are Vitamin B12 and Folate Deficiency Clinically Important After Roux-en-Y Gastric Bypass?

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Although iron, vitamin B12, and folate deficiency have been well documented after gastric bypass operations performed for morbid obesity, there is surprisingly little information on either the natural course or the treatment of these deficiencies in Roux-en-Y gastric bypass (RYGB) patients. During a 10-year period, a complete blood count and serum levels of iron, total iron-binding capacity, vitamin B12, and folate were obtained in 348 patients preoperatively and postoperatively at 6-month intervals for the first 2 years, then annually thereafter. The principal objectives of this study were to determine how readily patients who developed metabolic deficiencies after Roux-en-Y gastric bypass responded to postoperative supplements of the deficient micronutrient and to learn whether the risk of developing these deficiencies decreases over time. Hemoglobin and hematocrit levels were significantly decreased at all postoperative intervals in comparison to preoperative values. Moreover, at each successive interval through 5 years, hemoglobin and hematocrit were decreased significantly compared to the preceding interval. Folate levels were significantly increased compared to preoperative levels at all time intervals. Iron and vitamin B12 levels were lower than preoperative measurements and remained relatively stable postoperatively. Half of the low hemoglobin levels were not associated with iron deficiency. Taking multivitamin supplements resulted in a lower incidence of folate deficiency but did not prevent iron or vitamin B12 deficiency. Oral supplementation of iron and vitamin B12 corrected deficiencies in 43% and 81% of cases, respectively. Folate deficiency was almost always corrected with multivitamins alone. No patient had symptoms that could be attributed to either vitamin B12 or folate deficiency. Conversely, many patients had symptoms of iron deficiency and anemia. Lack of symptoms of vitamin B12 and folate deficiency suggests that these deficiencies are not clinically important after RYGB. Conversely, iron deficiency and anemia are potentially serious problems after RYGB, particularly in younger women. Hence, we recommend prophylactic oral iron supplements to premenopausal women who undergo RYGB. (J GASTROINTEST SURG 1998;2:436-442)

Patients who undergo Roux-en-Y gastric bypass (RYGB) for treatment of morbid obesity are prone to deficiencies in iron, vitamin B12, and folate. Although prophylactic multivitamin (MVI) supplements are routinely prescribed for RYGB patients, there are virtually no data in the medical literature demonstrating the efficacy of oral MVI supplements in prevention of either iron or vitamin B12 deficiency after RYGB. There is also a paucity of longitudinal data on the clinical consequences of metabolic deficiencies after RYGB. The primary goals of this study were to determine how readily patients with these deficiencies responded to postoperative supplementation of the deficient micronutrient and to learn whether the risk of developing these deficiencies decreases over time, which would suggest that the nonexcluded bowel eventually becomes more efficient in absorption of these substances. A secondary goal was to utilize this information to make recommendations for prophylaxis and treatment of the common metabolic sequelae of RYGB.

PATIENTS AND METHODS

We have followed several hematologic parameters in 348 patients who underwent RYGB during a 10-
year period including 321 patients who had a primary RYGB and 27 (7.7%) who had revision procedures. Our RYGB incorporated an upper pouch with a capacity of 30 ml or less with Roux limbs ranging from 50 to 150 cm in length. Limb length in this range does not affect the incidence of post-RYGB metabolic deficiencies. A complete blood count and serum levels of iron, total iron-binding capacity, vitamin B₁₂, and folate were obtained in each patient preoperatively. Postoperatively these tests were performed at 6-month intervals during the first 2 years and annually thereafter. Nearly all of these tests were performed in the laboratory at Robert Wood Johnson University Hospital, New Brunswick, New Jersey Postoperative follow-up and dietary counseling were carried out according to our usual protocol for patients who undergo RYGB at our institution. All patients were told to take a liquid or chewable MVI supplement daily during the first month. Most patients switched to a solid MVI supplement with minerals at 4 weeks postoperatively when the transition from pureed to solid food was completed.

Postoperative deficiencies were defined according to the following parameters: iron deficiency by serum levels below 45 μg/dl (normal = 45 to 135 μg/dl), vitamin B₁₂ deficiency by serum levels below 210 pg/dl (normal = 210 to 700 pg/dl), serum folate deficiency by levels below 4.0 ng/dl (normal = 4 to 16 ng/dl), and anemia by hemoglobin levels below 12.3 g/dl for women and 14.0 g/dl for men (normal = 12.3 to 15.5 g/dl for women and 14.0 to 16.2 g/dl for men). A positive response to treatment was defined as return of the value to a level at or above the lower limit of the normal range for our laboratory.

Postoperative laboratory results were collapsed into the following four time periods: the first 12 months (n = 305), the second 12 months (n = 215), 24 through 60 months (n = 175), and more than 60 months (n = 85). Mean length of follow-up was 42 ± 14 months and ranged from 6 to 128 months. Statistical analysis of data was performed using the chi-square test, unpaired Student’s t test, and two-way analysis of variance.

**RESULTS**

Table I shows the changes in the various hematologic parameters over time. Deficiencies were recognized in 268 (82%) of the 348 patients postoperatively including 155 patients (47%) with iron deficiency, 122 (37%) with vitamin B₁₂ deficiency, 115 (33%) with folate deficiency, and 177 (54%) with anemia. Hemoglobin and hematocrit values were significantly decreased compared to preoperative levels at all postoperative intervals. Moreover, at each successive postoperative interval through 5 years, hemoglobin and hematocrit were decreased significantly compared to the preceding interval. Conversely, serum iron levels remained relatively stable through the first 3 years postoperatively. Although mean iron levels at 36 months or more were significantly lower than at previous intervals, they remained well within the normal range. Changes in total iron-binding capacity were generally consistent with serum iron levels throughout the study. Although microcytic hypochromic indices were found in most anemic patients, only 63% of low iron levels were associated with microcytic indices. Moreover, 50% of low hemoglobin levels were not associated with iron deficiency. No patient had macrocytic anemia. Only three patients (0.8%) had macrocytic indices.

Fig 1 shows the changes in mean hemoglobin, iron, and vitamin B₁₂ values over time in 85 patients who were followed for 5 or more years. Postoperative changes in hematocrit were virtually the same as the pattern observed for hemoglobin. After 5 years both hemoglobin and hematocrit were increased relative to values obtained between 3 and 5 years postoperatively. Vitamin B₁₂ levels were more variable showing an initial decline during the first 24 months postoperatively.

<table>
<thead>
<tr>
<th>Time (mo)</th>
<th>No. of patients</th>
<th>Hemoglobin (g)</th>
<th>Hematocrit (%)</th>
<th>Iron (μg/dl)</th>
<th>TIBC (μg/dl)</th>
<th>Vitamin B₁₂ (pg/dl)</th>
<th>Folate (ng/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>348</td>
<td>13.8 ± 1</td>
<td>41.4 ± 4</td>
<td>79 ± 35</td>
<td>343 ± 61</td>
<td>450 ± 341</td>
<td>5.5 ± 3.4</td>
</tr>
<tr>
<td>Postoperative</td>
<td>12</td>
<td>304</td>
<td>13.2 ± 2*</td>
<td>39.5 ± 4*</td>
<td>74 ± 31</td>
<td>328 ± 62*</td>
<td>350 ± 205*</td>
</tr>
<tr>
<td>24</td>
<td>213</td>
<td>12.8 ± 2*</td>
<td>38.4 ± 5*</td>
<td>77 ± 37</td>
<td>352 ± 73</td>
<td>337 ± 192*</td>
<td>9.0 ± 6.3*</td>
</tr>
<tr>
<td>≥36</td>
<td>195</td>
<td>12.4 ± 2*</td>
<td>37.7 ± 5*</td>
<td>65 ± 36*</td>
<td>378 ± 73*</td>
<td>357 ± 217*</td>
<td>9.2 ± 5.2*</td>
</tr>
</tbody>
</table>

TIBC = total iron-binding capacity

Data are expressed as mean ± standard deviation

* Significant difference vs. preoperative measurement (P < 0.05 by analyses of variance with Student's-Newman-Keuls test)

† Significant difference vs. the preceding time interval(s) (P < 0.05 by analysis of variance with Student's-Newman-Keuls test)