Obesity Surgery (2019) 29:3818–3823
https://doi.org/10.1007/s11695-019-04070-5

ORIGINAL CONTRIBUTIONS

Is Transdermal Multivitamin Patch Effective in Gastric Bypass Patients?

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Published online: 13 July 2019

Abstract

Background Laparoscopic Roux-en-Y gastric bypass (LRYGB) patients are recommended to take multiple oral vitamin supplements daily. Transdermal multivitamin patches are being advertised as an alternative for use in bariatric patients with no data to support their efficacy. The purpose of this study was to evaluate response to daily transdermal use of multivitamin patch after LRYGB and to compare them with a control group of similar patients who used oral supplements.

Methods A retrospective review was carried out on patients who had LRYGB at a community hospital from February 2015 to February 2019. Patients who had completed preoperative and annual postoperative bariatric laboratory tests were included. They were divided into patch and pill (control) group.

Results Seventeen patients were included in the patch and 27 in the pill group. Patients in each group used either patch or pills for 12 months and they were 1 year post LRYGB. Fourteen patients (82.35%) in patch group and 11 patients (40.74%) in pill group had at least 1 deficiency at annual postoperative blood work ($P = .0116$). Vitamin D deficiency was seen in 81% patients in patch group vs 36% in the pill group ($P = .0092$). Statistically significant lower postoperative serum concentrations of vitamin D, B1, and B12 were seen in the patch group.

Conclusions Multivitamin patch users are more likely to have vitamin D deficiency and lower serum concentration of various vitamins and minerals. Future large studies are needed on the efficacy of multivitamin patches before they can be recommended to bariatric patient population.

Keywords Laparoscopic Roux-en-Y gastric bypass · Bariatric surgery · Vitamin deficiency · Transdermal multivitamin patch · Oral vitamins

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Introduction

Laparoscopic Roux-en-Y gastric bypass (LRYGB) is a commonly performed bariatric surgery. It is associated with increased risk of vitamin and mineral deficiencies due to calorie restriction and bypass of upper intestinal tract. Commonly diagnosed post-surgery deficiencies in these patients include vitamin D (20%–51%), vitamin B12 (37%–50%), iron (47%–66%), folate (15%–38%), and calcium (±10%) [1–7]. The updated 2016 nutritional guidelines from American Society for Metabolic and Bariatric Surgery (ASMBS) recommend daily use of multivitamin and mineral supplements to avoid these deficiencies [8]. Standard multivitamin supplements include oral intake of multiple pills daily. Many patients do not like taking multiple pills daily and have difficulty remaining compliant with their intake. Standard multivitamin supplements intake has been found to be not very effective in avoiding vitamin deficiencies after bariatric surgery primarily

due to non-compliance issue [2, 9, 10]. Transdermal multivitamin patch is being advertised as an alternative for use in bariatric surgery patients. Table 1 shows vitamins and minerals amount present in each Patch MD multivitamin plus patch and its comparison with the recommended dietary allowances (RDA) made by ASMBS. Compliance can be better since it is used once a day. There is no published study looking at the efficacy of nutrient delivery via a vitamin and mineral patch in post bariatric surgery patients. The purpose of this study was to evaluate response to daily transdermal use of Patch MD multivitamin patch in patients after LRYGB by identifying how many of these patients develop deficiencies, measuring blood levels of various micronutrients, and comparing them with a control group of similar patients who used oral multivitamin supplements.

Methods

After institutional review board approval, a retrospective chart review was carried out on patients who had LRYGB by a single surgeon at a community hospital from February 2015 to February 2019. Patients who had completed preoperative and annual 1 year postoperative bariatric blood work were included in the study. Patients were excluded if they had other bariatric surgery like sleeve gastrectomy or revisional surgery and had not completed annual postoperative bariatric blood work. Patients who used Patch MD multivitamin plus patch for 12 months were included in the case group. Patients who took oral multivitamin supplements for 12 months were included in the control group. All the patients in the patch and pill groups were 1 year post LRYGB. Data collected using electronic medical record included age, gender, ethnicity, preoperative body mass index (BMI), 1 year postoperative BMI, percent excess weight loss (% EWL—defined as weight loss divided by excess weight based on ideal weight at BMI 25 kg/m^2 × 100), percent total weight loss (% TWL—defined as weight loss divided by initial weight × 100), location patch was applied, preoperative and postoperative serum concentration of vitamin D, vitamin, B1, vitamin B12, folate, ferritin, calcium, and hemoglobin.

All postoperative gastric bypass patients were recommended to take 2 chewable multivitamins, 1 oral vitamin B12 (500 mcg), 1 vitamin B complex, 1 iron (iron 65 mg or ferrous sulfate 325 mg), 3 calcium with vitamin D (600 mg calcium/800 IU vitamin D), 1 vitamin D (100 IU) supplements daily based on our bariatric program guidelines. Patients who did not like taking oral vitamin supplement starting using Patch MD multivitamin plus patch daily at their own discretion.

The primary outcome was comparison of the percentage of patients who had at least 1 or more number of vitamin or minerals deficiencies at 1 year after surgery. Secondary outcome was average decrease in serum vitamin and mineral concentrations at 1 year postoperative blood work. Secondary outcomes also included change in BMI, % EWL, and % TWL. Deficiencies for vitamins and minerals were defined as a value under the lower limit of normal according to our laboratory references.

All surgeries were performed by 1 surgeon using the same technique. LRYGB was performed in an anticolic, antigastric

Table 1 Demonstrates supplements amount in each Patch MD multivitamin plus topical patch

Vitamins/minerals	Amount per patch	% RDA	Vitamins/minerals	Amount per patch	% RDA
Vitamin A	10000 IU	100%	Calcium	1500 mg	100%
Vitamin C	1000 mg	NA	Iron	45 mg	100%
Vitamin D3	5000 IU	167%	Phosphorus	100 mg	NA
Vitamin E	200 IU/134 mg	893%	Iodine	150 μg	NA
Vitamin K2	160 μg	133%	Magnesium	500 mg	NA
Vitamin B1	25 mg	100%	Zinc	15 mg	100%
Vitamin B2	25 mg	NA	Selenium	100 μg	NA
Vitamin B3	40 mg	NA	Copper	2 mg	100%
Vitamin B6	25 mg	NA	Manganese	4 mg	NA
Vitamin B9 (Folic acid)	400 μg	100%	Chromium	200 μg	NA
Vitamin B12	1000 μg	200%	Molybdenum	100 μg	NA
Biotin	600 μg	NA	Potassium	99 mg	NA
Pantothenic acid	25 mg	NA	Chloride	70 mg	NA
Boron	3 mg	NA			

% RDA, recommended dietary allowances per American Society for Metabolic and Bariatric Surgery (ASMBS) Guidelines; NA, recommendations not available

fashion. The biliopancreatic limb and roux limb were 30 cm and 100 cm in length, respectively. Linear staplers were used to create gastrojejunal and jejunojejunal anastomosis.

Categorical variables between the two groups were compared using the chi-square test or Fisher's exact test and continuous variables using Student's *t* test. Results were presented as mean (range). When pre and post comparison was done within the same group, paired *t* test was used. A *P* value of < .05 was considered to be statistically significant.

Results

A total of 104 patients had LRYGB from February 2015 to February 2019. Forty-four of these patients met the inclusion criteria. Thirteen patients were lost to follow up. Four patients who used patch were 2-year post LRYGB and were not included in the study. Forty-three patients had LRYGB after February 2018 and had not completed their 1 year postoperative follow up at the completion of the study. The included patients were divided into the patch and the pill (control) group and included 17 and 27 patients, respectively. The mean age for the patch group was 43.2 years (range, 34–61) and for the pill group was 48.96 years (range, 38–65, $P = 0.0273$). In the patch group 16 (94%), patients were female and there were 19 (70%) females in the control group ($P = 0.121$) (Table 2). Caucasians accounted for 16 (94%) and 24 (89%) patients in the 2 groups, respectively.

The corresponding mean preoperative BMI was 44.67 (range, 35.7–50.8) and 43.14 (36.5–51.4) kg/m^2 respectively in the patch and pill group ($P = 0.2$). The 1 year postoperative BMI for patch group was 30.2 and pill group was 31.47 kg/m^2 ($P = 0.3056$). The % EWL loss for patch and pill group was 75% (54–125%) and 67% (30–100%), respectively ($P = 0.1874$). The % TWL loss for patch and pill group was 33% (20–52%) and 27% (10–40%), respectively ($P = 0.012$). There was no statistically significant difference in BMI change and % EWL between the 2 groups; however, the patch group had a statistically significant higher % TWL.

In the patch group, 16 patients only used Patch MD multivitamin plus patch. One patient used additional endurance max plus topical patch daily. The patch was applied to the arm, chest wall, or abdominal wall.

At least one deficiency was seen in 14 out of 17 patients (82.35%) in the patch group and 11 out of 27 patients (40.74%) in the pill group ($P = 0.0116$). The patients in the patch group were more likely to have at least 1 vitamin/mineral deficiency and this was statistically significant. Two or more deficiencies were seen in 4 (23.5%) and 2 patients (7.4%) respectively in the two groups ($P = 0.1857$).

Vitamin D deficiency was the most common deficiency seen in both groups. Preoperative vitamin D deficiency was seen in 2 out of 2 patients (100%) in the patch group and 11 out of 18 patients (61%) in the pill group. A significantly increased number of patients in the patch group had vitamin D deficiency on the annual postoperative blood work. Thirteen (81.2%) patients in the patch group and 9 (36%) patients in the pill group had vitamin D deficiency ($P = 0.0092$). Preoperative vitamin D levels were not performed in most of the patients due to insurance issues (Table 3).

Vitamin B12 deficiency was only seen in one patient in the patch group. Pill group had no deficiency in vitamin B1, vitamin B12, and folate. Patch group also had no vitamin B1 and folate deficiency.

In the patch group, there was no statistically significant difference in serum concentration of preoperative and postoperative vitamin D, vitamin B12, folate, ferritin, and calcium. Vitamin B1 and hemoglobin levels were lower at 1 year postoperative blood draw and it was statistically significant (Table 3).

In the pill group, a statistically significant increase in postoperative serum concentration of vitamin B1 (172.6 vs 127.1 nmol/l, $P = 0.0016$), vitamin B12 (759 vs 483.2 pg/ml, $P = 0.0016$), vitamin D (33.52 vs 26.2 ng/ml, $P = 0.0007$), and folate (16.4 vs 14.4 ng/ml, $P = 0.0345$) was seen as compared with preoperative levels (Table 4).

Comparison of postoperative serum concentration of vitamins/minerals between the 2 groups showed a significantly higher levels of vitamin B1 (172.6 vs 134.29 nmol/l, $P = 0.0087$), vitamin B12 (759 vs 504.64 pg/ml, $P = 0.0119$), and vitamin D (33.52 vs 23.93 ng/ml, $P = 0.0019$) in the pill group (Table 5). Folate (16.4 vs 13.65 ng/ml, $P = 0.0752$) and ferritin (89.2 vs 84.49 ng/ml, $P = 0.8657$) levels were also higher in the pill group; however, it was not statistically significant.

Discussion

Essential micronutrients are those nutrients that cannot be synthesized by humans. These micronutrients include water-soluble and fat-soluble vitamins, and trace elements. A significant deficiency of an essential micronutrient can induce a clinical syndrome. Prevention, diagnosis, and treatment of these deficiencies are necessary parts of lifelong care after bariatric surgery.

Multiple oral vitamin and mineral supplements are recommended after bariatric surgery to avoid various deficiencies. After, LRYGB patients may be asked to take anywhere from 6 to 10 pills daily. Compliance with intake of oral multivitamin supplements is an issue in patients after LRYGB. Brolin et al. reported only 33% patients to be compliant with daily multivitamin intake after Roux-en-Y gastric bypass (RYGB) over a 5-year period [6].

A large number of multivitamin patches are being advertised as an alternative for use in bariatric surgery patients. The advantages stressed by the companies include better

Table 2 Demonstrates comparison of demographics and postoperative deficiencies between patch and pill group

	Patch group	Pill group	*P* value
Number of patients	17	27	
Age (years)	43.2 (34–61)	49 (38–65)	0.0199
Male/female ratio	1/16 (94% Female)	8/19 (70% female)	0.1215
Preoperative BMI (kg/m^2)	44.67 (35.7–50.8)	43.1 (36.5–51.4)	0.2000
1 year postoperative BMI (kg/m^2)	30.2 (20.6–36.9)	31.4 (25.3–40.5)	0.3056
% EWL	75% (54–125%)	67% (30–100%)	0.1874
% TWL	33% (20–52%)	27% (10–40%)	0.0120
Duration patch or oral vitamins were used (months)	12	12.22	0.3265
Postoperative deficiencies (*N*, %)			
1 deficiency	14/17 (82.35%)	11/27 (40.74%)	0.0116
2 or more deficiency	4/17 (23.5%)	2/27 (7.4%)	0.1857
Vitamin D (< 30 ng/ml)	13/16, 81.2%	9/25, 36%	0.0092
Vitamin B12 (< 211 pg/ml)	1/17, 5.88%	0/27, 0%	0.3864
Vitamin B1 (< 78 nmol/l)	0/17, 0%	0/27, 0%	NA
Folate (< 4.4 ng/ml)	0/16, 0%	0/25, 0%	NA
Ferritin (< 13 ng/ml)	3/17, 17.65%	1/27, 3.7%	0.2821
Hemoglobin (< 12 g/dl)	2/17, 11.76%	2/26, 7.7%	1
Calcium (< 8.6 mg/dl)	1/17, 5.88%	1/27, 3.7%	1

Data is presented as mean (range) or *N* (%)

BMI, body mass index; *% EWL*, percent excess weight loss; *% TWL*, percent total weight loss

compliance due to once a day application and avoiding gastrointestinal system upset. It is also stressed that they provide more than the required vitamins and minerals dose recommended in post bariatric surgery patients. There is no data available regarding transdermal vitamin patches efficacy in bariatric surgery patients. Some of our patients had started using Patch MD multivitamin patches as they did not want to take oral vitamin supplements. To evaluate the effectiveness of these multivitamin patches, we compared the annual postoperative vitamin and mineral levels of these patients with the ones who were on oral supplements.

The mechanism of action of these multivitamin patches is not well understood. Low lipophilic transdermal permeability makes it a challenge to deliver vitamins transdermally [11]. Multiple penetration enhancers are being used to enhance the delivery across stratum corneum of the epidermis. Radiation from either an Er:YAG (erbium-doped yttrium aluminum garnet) or a CO2 laser and microdermabrasion have been shown to enhance transdermal penetration of vitamin C derivatives in vitro [11]. Hutton et al. demonstrated vitamin K delivery using dissolving type microneedles in neonatal porcine skin [12]. Alsaqr et al. studied transdermal delivery of vitamin D3 in porcine skin using different chemical penetration enhancers. Ointment was used as transdermal delivery system. There results showed that daily recommended vitamin D3 dose (400 IU or 10 μg) can be achieved by covering a surface of the skin of 3.6 × 3.6 cm with vitamin D3 ointment containing both ethanol and dodecyclamine [13]. Kim et al. showed successful transdermal delivery of vitamin D3 using coated microneedles in a porcine skin model. They showed that plasma concentration of vitamin D3 to be better than ointment based transdermal method [14].

There are no published studies looking at the efficacy of patches in delivering vitamins and minerals in bariatric

Table 3 Demonstrates in the patch group comparison between preoperative and 1 year postoperative vitamins/minerals serum concentration

Vitamins/minerals—PATCH (normal range)	Preoperative levels	1 year postoperative levels	*P* value
Vitamin D, 25-OH, total (30–100 ng/ml)	21.5 (21–22)	23.93 (12–39)	0.7284
Vitamin B12 (211–946 pg/ml)	523.88 (266–788)	504.64 (172–868)	0.7188
Vitamin B1 (78–185 nmol/l)	152.94 (106–233)	134.29 (84–198)	0.0422
Folate (4.4–31 ng/ml)	14.24 (7–20)	13.65 (5.6–20)	0.6496
Ferritin (13–150 ng/ml)	102.88 (11–330)	84.49 (10–444)	0.1807
Calcium (8.6–10.5 mg/dl)	9.25 (8.7–10.2)	9.28 (8.4–9.7)	0.7108
Hemoglobin (12–16 g/dl)	13.83 (12.1–15.5)	13.47 (11.7–15.2)	0.0461

Data is presented as mean (range)

Table 4 Demonstrates in the pill group comparison between preoperative and 1 year postoperative vitamins/minerals serum concentration

Vitamins/minerals—PILLS (normal range)	Preoperative levels	1 year postoperative levels	*P* value
Vitamin D, 25-OH, total (30–100 ng/ml)	26.2 (13–52)	33.52 (17–57)	0.0007
Vitamin B12 (211–946 pg/ml)	483.2 (176–917)	759 (289–2000)	0.0016
Vitamin B1 (78–185 nmol/l)	127.1 (84–180)	172.6 (96–343)	0.0016
Folate (4.4–31 ng/ml)	14.4 (7.7–20)	16.4 (6.5–20)	0.0345
Ferritin (13–150 ng/ml)	97.8 (15–335)	89.2 (12–207)	0.3865
Calcium (8.6–10.5 mg/dl)	9.3 (8.3–10.1)	9.21 (8.5–9.8)	0.1166
Hemoglobin (12–16 g/dl)	13.3 (11.2–15.2)	13.41 (11.2–15.6)	0.5339

Data is presented as mean (range)

surgery patients. There are 2 ongoing trials looking at serum vitamin and mineral concentration in bariatric surgery patients using transdermal vitamin patches; however, the results have not yet been published [15, 16].

Toh et al.'s study showed that 1 year after Roux-en-Y gastric bypass (RYGB) in patients on multiple oral vitamin supplements, the prevalence of vitamin D deficiency is 30%, low ferritin level is 15%, low iron is 21%, low hemoglobin is 17%, low vitamin B12 is 11%, and low folate is 12% [17]. In patients presenting for bariatric surgery, vitamin D deficiency is the most common deficiency and can be seen in 57–80% patients preoperatively [17–19]. Vitamin D deficiency after LRYGB is probably due to bypass of proximal small intestine where it usually gets absorbed [1]. Obesity itself seems to be a risk factor in developing vitamin D deficiency [2]. In our study, vitamin D was the most common deficiency in both preoperative and postoperative blood work. Patients using multivitamin patch appear to have a significantly higher risk of developing Vitamin D deficiency as compared with those taking pills. Even the postoperative serum concentration of vitamin D is significantly lower in patch group patients.

Preoperative vitamin B12 deficiency can be seen in up to 9% of obese patients [2]. LRYGB can cause vitamin B12 deficiency by decreasing the levels of acid, pepsin, and pancreatic enzymes which are required to release vitamin B12 bound to proteins in food. Reduction in availability of intrinsic factors produced by the parietal cells of the stomach can also affect vitamin B12 absorption [2, 17]. Vargas-Ruiz et al. demonstrated an incidence of vitamin B12 deficiency after RYGB in patients on oral multivitamin supplements to be 10% at 1 year, 16.6% at 2 years, and 18% at 3 years [20]. In our study, vitamin B12 deficiency was very rare and seen preoperatively in only 2 out of 44 patients (4.5%). In the postoperative period, only 1 patient in the patch group had vitamin B12 deficiency. The postoperative serum concentration of vitamin B12 was significantly lower in patch group as compared with pill group.

Vitamin B1 (thiamin) deficiency after LRYGB is uncommon but can cause serious and permanent side effects like Wernicke's encephalopathy. Intractable vomiting, restriction in energy intake, and malabsorption after LRYGB can increase the risk of thiamin deficiency [21]. In our study, there was no patient with vitamin B1 deficiency on the preoperative and postoperative blood work. However, the patch group patients had a significantly lower postoperative serum concentration of vitamin B1 as compared with pill group patients.

The main factors for iron deficiency after gastric bypass include malabsorption due to bypass of duodenum and proximal jejunum, reduction of food intake, and intolerance to iron-rich food like beef [2, 3, 17]. Serum ferritin is the gold standard in diagnosing iron deficiency. Twenty to 49% patients after RYGB have been reported to have iron deficiency. Folate deficiency can be seen in 0–18% of these patients [3]. In our study, ferritin deficiency was more common in patch group. Serum ferritin and folate levels were lower in the patch group; however, it was not statistically significant. Calcium and hemoglobin levels showed no significant difference between the 2 groups.

Table 5 Comparison of 1 year postoperative serum concentration of vitamins/minerals in the patch and pill group

Postoperative mean serum concentration (normal range)	Patch group	Pill group	*P* value
Vitamin D, 25-OH, total (30–100 ng/ml)	23.93 (12–39)	33.52 (17–57)	0.0019
Vitamin B12 (211–946 pg/ml)	504.64 (172–868)	759 (289–2000)	0.0119
Vitamin B1 (78–185 nmol/l)	134.29 (84–198)	172.6 (96–343)	0.0087
Folate (4.4–31 ng/ml)	13.65 (5.6–20)	16.4 (6.5–20)	0.0752
Ferritin (13–150 ng/ml)	84.49 (10–444)	89.2 (12–207)	0.8657
Calcium (8.6–10.5 mg/dl)	9.28 (8.4–9.7)	9.21 (8.5–9.8)	0.4958
Hemoglobin (12–16 g/dl)	13.47 (11.7–15.2)	13.41 (11.2–15.6)	0.8870

Data is presented as mean (range)

The limitation of this study is that it is a retrospective analysis from a single center with small sample size. The compliance to use of patch and pills in our study could not be assessed. Despite its limitations, our study is the first to evaluate the efficacy of transdermal multivitamin patch in post LRYGB patients. Future larger, multicenter prospective studies are needed to evaluate the efficacy of multivitamin transdermal patch and the effect of various variables like age, gender, ethnicity, weight loss, and skin thickness on its effectiveness in bariatric surgery patients.

Conclusion

Our study shows that transdermal multivitamins are not as effective as oral vitamin supplements. Patients using Patch MD multivitamin patch are more likely to have vitamin D deficiency and also have lower serum concentration of vitamin D, vitamin B1, vitamin B12, folate, and ferritin. Larger multicenter prospective studies are needed before its use can be recommended in post LRYGB patients.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent For this type of study, formal consent is not required.

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