Published in final edited form as:

Surg Obes Relat Dis. 2019 September ; 15(9): 1503–1504. doi:10.1016/j.soard.2019.07.016.

Comment on: Micronutrient intake and biochemistry in adolescents adherent or nonadherent to supplements 5 years after Roux-en-Y gastric bypass surgery

Jaime M. Moore, M.D.,

University of Colorado School of Medicine, Aurora, Colorado

Nancy F. Krebs, M.S., M.D.

University of Colorado School of Medicine, Aurora, Colorado

Micronutrients are like the stage crew in a play—silently orchestrating countless essential functions, but without the bravado of the lead actors (i.e., weight loss, co-morbidity improvement). As such, they require careful attention and respect so the show can go on.

In this article, Henfridsson et al. [1] present a valuable assessment of the longitudinal intake, adherence, and status of micronutrients through 5 years after Roux-en-Y gastric bypass among adolescents in the multicenter Swedish Adolescent Morbid Obesity Surgery study. One notable strength of the Swedish Adolescent Morbid Obesity Surgery study design is its inclusion of a nonsurgical, matched control group, which is particularly helpful when characterizing micronutrient deficiencies that are prevalent in the general population, and particularly among individuals with obesity (e.g., vitamin D).

The data provide another practical reminder to temper our expectations of adolescents' adherence to oral micronutrient supplementation after bariatric surgery. The reported overall adherence of approximately 50% is likely even lower after factoring in the social desirability bias inherent in self-reported data. Additionally, without a standardized definition of adherence (here 3 d/wk), this construct is difficult to compare across studies [2]. "True" adherence to micronutrient supplementation in this population was perhaps most objectively measured by Modi et al. [3], who used an electronic medication cap monitoring system to track a subset of adolescents in the Teen Longitudinal Assessment of Bariatric Surgery study for the first 6 months postoperatively. Those authors found a mean measured adherence of 27% at 6 months (versus the self-reported 79% at the same time point). It is worth noting that the 2 major barriers identified to taking supplementation in the Modi study were (1) forgetting and (2) difficulty swallowing pills. Given that nonadherence to oral supplementation is an exceedingly common risk factor for developing micronutrient deficiencies in this population (with no credible prospect for improvement), it is logical to shift our attention to the development and study of alternative, cost-effective strategies for micronutrient delivery to address these known barriers. Intramuscular injection of Vitamin B12 is 1 example of how a nonoral route for a micronutrient has been successfully integrated into routine postbariatric clinical care.

Alternative routes of administration to consider to prevent or treat micronutrient deficiencies in this setting include intravenous infusions (e.g., for iron) and transdermal delivery (via

patch or emerging microneedle technology [4]). Intravenous iron infusions have long been used in patients with chronic kidney disease, with a growing evidence base for safety and efficacy in nonrenal conditions [5,6]. Compared with oral iron, intravenous iron is associated with fewer gastrointestinal side effects, superior absorption by bypassing the regulator hepcidin, and current formulations have greatly improved safety profiles compared with older dextran-containing products [7]. Another option may be to use more potent forms of oral supplementation (e.g., heme iron versus traditional nonheme ferrous sulfate/fumarate/gluconate), which could result in better accepted (e.g., once weekly) dosing regimens. Absorption of a multivitamin-containing transdermal patch in the post-bariatric surgery setting is currently being evaluated in a single-center observational study in adults ([ClinicalTrials.gov](https://clinicaltrials.gov)).

Next, the present study offers further evidence for the strikingly high prevalence of iron deficiency (with and without anemia) that has been consistently observed among adolescents of both sexes after bariatric surgery, and which progresses over time [8]. At 5 years in this study, 61% of all females had a ferritin level $<15 \mu\text{g/L}$, 41% of whom were anemic, and 62% of males had a ferritin level $<30 \mu\text{g/L}$, 15% of whom were anemic. In adults, iron (heme and nonheme) absorption has been shown to be significantly and equally impaired after sleeve gastrectomy and gastric bypass at 1 year [9]. Potential clinical consequences of iron deficiency include disturbances in energy, cognition, mood/behavior, and sleep, all of which can undermine efforts to achieve ongoing weight loss/weight maintenance, cardiometabolic improvement, and psychosocial risk reduction. Unfortunately, the authors in this study did not collect data about how micronutrient deficiencies, once identified, were treated. Thus, how responsive or refractory this iron deficiency is to standard therapy is unknown and warrants additional study.

Adolescence is a period defined by emerging autonomy and dynamic growth (of bone, muscle, and blood volume), during which iron needs are estimated to double in both sexes [10]. In the 2018 Pediatric Metabolic and Bariatric Surgery guidelines, the removal of the requirement for adolescents to achieve close to their adult height by bone age or Tanner staging presumably will increase the proportion of younger medically appropriate candidates for bariatric surgery [11]. Young women will specifically be at risk for additional health consequences if iron deficiency and anemia persist into pregnancy. The current American Society for Metabolic and Bariatric Surgery Integrated Health Nutritional Guideline on Micronutrients does not provide specific recommendations for adolescents, and iron is just one example for which extrapolating this adult guideline to an adolescent population should not be expected to be accurate [12]. Accordingly, we should work toward establishing specific micronutrient guidelines for adolescents, accounting for their unique physiology and evolving maturation of executive function.

Remaining issues to be addressed that have the potential to improve the precision and effectiveness of our approach to micronutrient management postoperatively include the following: understanding how absorption/homeostatic regulation of micronutrients is altered in adolescents, evaluating the impact of procedure type on the underlying mechanisms of deficiencies and on treatment response, and improving education and support for primary

care providers to enhance knowledge and self-efficacy in the recognition of micronutrient deficiencies in between nutrition/bariatric specialty care visits.

While the initial signs and symptoms of the micronutrient deficiencies highlighted in this study may be subclinical or nonspecific, they can still impact quality of life, and if not detected early, can progress to pathology that can be difficult and more costly to treat (e.g., fractures, anemia). Understanding, preventing, and treating deficiencies after bariatric surgery in a way that is tailored to adolescents with strategies that move beyond the daily pill paradigm may make the difference between producing a mediocre show versus a long-running hit.

References

- [1]. Henfridsson P, Laurenius A, Wallengren O, et al. Micronutrient intake and biochemistry in adolescents adherent or nonadherent to supplements 5 years after Roux-en-Y gastric bypass surgery. *Surg Obes Relat Dis* 2019;15(9):1494–504. [PubMed: 31371184]
- [2]. Hood MM, Kelly MC, Feig EH, Webb V, Bradley LE, Corsica J. Measurement of adherence in bariatric surgery: a systematic review. *Surg Obes Relat Dis* 2018;14(8):1192–201. [PubMed: 29853195]
- [3]. Modi AC, Zeller MH, Xanthakos SA, Jenkins TM, Inge TH. Adherence to vitamin supplementation following adolescent bariatric surgery. *Obesity (Silver Spring)* 2013;21(3):E190–5. [PubMed: 23404956]
- [4]. Maurya A, Nanjappa SH, Honnavar S, Salwa M, Murthy SN. Rapidly dissolving microneedle patches for transdermal iron replenishment therapy. *J Pharm Sci* 2018;107(6):1642–7. [PubMed: 29462631]
- [5]. Crary SE, Hall K, Buchanan GR. Intravenous iron sucrose for children with iron deficiency failing to respond to oral iron therapy. *Pediatr Blood Cancer* 2011;56(4):615–9. [PubMed: 21298748]
- [6]. Stein RE, Plantz K, Maxwell EC, Mamula P, Baldassano RN. Intravenous iron sucrose for treatment of iron deficiency anemia in pediatric inflammatory bowel disease. *J Pediatr Gastroenterol Nutr* 2018;66(2):e51–5. [PubMed: 28704225]
- [7]. Goldstein SL, Morris D, Warady BA. Comparison of the safety and efficacy of 3 iron sucrose iron maintenance regimens in children, adolescents, and young adults with CKD: a randomized controlled trial. *Am J Kidney Dis* 2013;61(4):588–97. [PubMed: 23245582]
- [8]. Ruiz-Cota P, Bacardí-Gascón M, Jiménez-Cruz A. Long-term outcomes of metabolic and bariatric surgery in adolescents with severe obesity with a follow-up of at least 5 years: a systematic review. *Surg Obes Relat Dis* 2019;15(1):133–44. [PubMed: 30514669]
- [9]. Ruz M, Carrasco F, Rojas P, et al. Heme- and nonheme-iron absorption and iron status 12 mo after sleeve gastrectomy and Roux-en-Y gastric bypass in morbidly obese women. *Am J Clin Nutr* 2012;96(4):810–7. [PubMed: 22952172]
- [10]. Beard JL. Iron requirements in adolescent females. *J Nutr* 2000;130(2 Suppl):440S–2S. [PubMed: 10721923]
- [11]. Pratt JSA, Browne A, Browne NT, et al. ASMBS pediatric metabolic and bariatric surgery guidelines, 2018. *Surg Obes Relat Dis* 2018;14(7):882–901. [PubMed: 30077361]
- [12]. Parrott J, Frank L, Rabena R, Craggs-Dino L, Isom KA, Greiman L. American Society for Metabolic and Bariatric Surgery integrated health nutritional guidelines for the surgical weight loss patient 2016 update: micronutrients. *Surg Obes Relat Dis* 2017;13(5):727–41. 10.1016/j.soard.2019.07.016 [PubMed: 28392254]