Exploring Vitamin B12 Deficiency in Sleeve Gastrectomy from a Histological Study of a Cadaveric Stomach and Ileum

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Keywords: Vitamin B12 Deficiency; Bariatric surgery; Gastrectomy

Introduction

Of the two broad categories of Bariatric surgery, gastric banding and gastric stapling, the latter is more permanent as it removes or seals off part of the stomach. The 2 most common type of gastric stapling is Roux-en-Y Gastric Bypasses (RYGB) as compared to those post-Sleeve Gastrectomies (SG). From 2008 to 2011, SG procedures jumped roughly 80% to 94,689 whereas RYGB procedures actually saw a decline by 7% [1].

Interestingly, nutritional assessment, either through meta-analysis [3] or through pilot studies that were done worldwide including the United States [4], United Kingdom [5], and Greece [6], suggests a similar finding when it comes to deficiency of Vitamin B12 in patients after their procedures. B12 Deficiency is more commonly found amongst patients who have undergone RYGB as compared to that post-SG [3-6].

Surgically, the major difference between SG and RYGB is that the latter greatly bypasses the physiological functions of the stomach, whereas the former keeps the stomach intact but by vastly reducing its size [2]. Since the stomach is the major variable in the two procedures and plays an important role in B12 absorption as seen in Figure 1a, we hypothesize that the stomach has the ability to regenerate and increase its surface area to compensate for the loss of its volume in SG patients.

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Of the chronic complications for SG, nutritional deficiencies are of particular interest, since fewer such incidences are reported post-SG compared to post-RYGB [2]. Transformation of any part of the GI tract could have adverse effects on the body's absorption capability of nutrients including that of Vitamin B12 or Cobalamin. Deficiency in Vitamin B12 can cause pernicious anemia, which can lead to fatigue and memory loss along with palpatitations, dizziness, loss of appetite, numbness, vision loss, and depression.

Abstract

Introduction: Vitamin B12 Deficiency is more commonly found amongst patients who have undergone Roux-en-Y Gastric Bypasses (RYGB) as compared to those post-Sleeve Gastrectomies (SG). The major difference between SG and RYGB is that the latter greatly bypasses the stomach, whereas the former simply reduces the gastric volume.

Purpose: The aim of this paper is to study the stomach and distal ileum, histologically, in a cadaver with SG to explain the higher rate of incidences of B12 deficiency seen in patient's post-RYGB relative to patient's post-SG. Since the stomach is the major variable in the two procedures, we hypothesize that it has the ability to regenerate and increase its surface area to compensate for the loss of its volume in SG patients.

Material and Methods: Tissue biopsies and Hematoxylin and Eosin stains were performed from various anatomical locations of the GI tract, specifically, the fundus, the body, and the antrum of the stomach and from the distal ileum of the small intestine of a cadaver with SG and one without (control).

Results: Compared to the control, the SG cadaver's gastric tissue biopsies were significant for chronic gastritis and hypertrophy of the muscularis externa layer. More importantly, parietal cell hyperplasia and deeper mucosal glands were also noted in the SG cadaver supporting the hypothesis.

Conclusion: The compensatory role of an intact stomach, given its ability to regenerate parietal cells and increase its number in the gastric fundus and body, can be better appreciated in a gastric-sparing procedure such as SG versus RYGB in terms of limiting B12 deficiencies.

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difference seen in B12 deficiency between patients post-SG vs. post-RYGB (Figure 1d). The study will help answer two questions: does the body have the ability to compensate for a reduced gastric size and if so, then how?

Subjects and Methods

Specimen were collected from two cadavers provided by the Anatomy Department of the Ross University School of Medicine. The cadaver with the SG belonged to a 66-year-old obese male whose cause of death (COD) on record was dementia. The cadaver used as a Control belonged to a 76-year-old obese male whose COD on record was a subdural hematoma. Neither patient had any reported history of Vitamin B12 Deficiency. Past medical history and COD is limited to the information provided above. Tissue biopsies were performed at various anatomical locations as seen in Figure 1c from the GI tract, specifically, the gastric fundus, body (both the greater curvature and the lesser curvature), and antrum and from the distal ileum of the small intestine of both cadavers simultaneously to control for postmortem variables.

Tissue processing and staining protocols set up by the Anatomy Department of Ross University School of Medicine were followed. To prepare the biopsy specimens for a histopathological comparison, they were dehydrated in ascending grades of alcohol and cleared in xylene, before being impregnated with molten paraffin and embedded in blocks. The blocks were left to cool at room temperature prior to being placed in a refrigerator to completely harden. Once solidified, cross sections of the tissues were made and placed on slides. The slides were stained with Hematoxylin and Eosin following proper H&E staining protocols and then differentiated and dehydrated in ascending alcohol concentrations. Coverslips were placed with mountant before being observed through a light microscope under varying magnifications.

Results

Histological cross sections of the gastric fundus, body, and antrum indicates chronic gastritis as evidenced by lymphocytes in the mucosal and submucosal layers (Figure 2a). Unlike the Control stomach, a very hypertrophic muscularis externa layer can be appreciated in all areas of the SG stomach under a 40X light microscopic magnification (Figure 2b). The SG stomach biopsies also had deeper pits and glands in the mucosal layer.

With higher magnification at 100X, chief cells (basophilic) and parietal cells (eosinophilic) were clearly identified and differentiated. Hyperplastic parietal cell distribution was noted overall and in particular around the neck (site between the pits and the glands) of the mucosal layers of the fundus and the body of the SG stomach (Figure 2c). The antrum of either the SG or the Control stomach did not have any parietal cell distribution (Figure 2d).

No major histological differences were noted in the distal ileum of either the SG or the Control's small intestine. Lastly, post-mortem tissue alterations including edema and other artifacts were taken into consideration and were deemed to have minimal to no effect on the observed findings.

Discussion

The stomach plays a crucial role in Vitamin B12 absorption. Parietal cells that line the neck of the mucosal glands (Figure 1c) of the gastric fundus and body releases Intrinsic Factor, which binds to B12 in the duodenum and is later recognized by receptors in the distal ileum of the small intestine (Figure 1a). Recognition of the Intrinsic Factors bound to B12 leads to absorption of B12 in the body [7-9].
Reduction of gastric volume in an SG procedure means a decrease in the number of parietal cells, which effectively limits the production of Intrinsic Factors required to adequately bind to B12 and avail it for absorption [10-13]. The body, therefore, remains in a compromised state of nutritional deficiency shortly after an SG procedure and requires supplemental therapy to prevent any adverse effects [2,10-13].

However, unlike in RYGB procedures where the entire stomach is bypassed, the stomach in SG procedures is actually utilized, albeit, at a smaller scope [2]. The higher incidence of B12 deficiency in patients after RYGB vs. in patients after SG suggests a unique ability of the stomach to overcome its newly downgraded state after an SG in a very significant way. Parietal cell hyperplasia along with an increased gastric surface area by means of deeper glands seen in a cadaver with SG provides evidence in support of this claim.

In fact, the increased distribution of parietal cells in the neck of the mucosal glands of only the gastric fundus and the gastric body is crucial to understanding the compensatory mechanism through which the human body deals with a decreased gastric volume. Stem cells that can differentiate into surface cells or gland cells are found in the neck of the mucosal glands of the stomach [7,14-16]. Short term B12 deficiency right after a procedure can trigger a response leading to stem cell differentiation into parietal cells, a renewal process that can take weeks [7,14,15]. Interestingly, parietal cells were not observed in the antrum of the SG stomach despite the body’s desire to respond. In normal histology, Parietal cells are only limited to the gastric fundus and body, whereas, most of the stem cells in the antrum are not programmed for such differentiation [7,14-16].

Although parietal cell hyperplasia as means of gastric compensation provides a compelling argument for the reduced incidences of B12 deficiencies after an SG procedure, alternative theories such as increased secretion of Intrinsic Factor from parietal cells or increased receptor-mediated endocytosis (absorption) of B12 in the distal ileum cannot be ruled out by this study. As such, the complete mechanism explaining gastric compensation for B12 deficiencies is not yet fully grasped and still needs to be studied further.

**Limitations and Further Studies**

There were various limitations to this report. Apart from the COD, access to only age and sex were available for either cadaver. Limited medical history of the subjects can blind this study from unforeseen variables, including age when SG was performed or of any prior history of Vitamin B12 Deficiencies. Given the use of cadavers for this study, clinical laboratory tests including blood level measurements for B12 and Methylmalonic Acid to determine B12 Deficiency, a Complete Blood Count to rule out pernicious anemia, and antibody titers against Intrinsic Factors and Parietal Cells for causation were not performed.

This study could be further enhanced with the addition of a post-RYGB cadaver as well as by increasing the number of overall cadaveric subjects. Additionally, tissue biopsies from living patients could limit any artefacts from post-mortem tissue alterations, however minimal they might have been in this study. Further studies using immunofluorescence staining to ascertain changes in the distal ileum would be helpful in further establishing the mechanism through which B12 Deficiency is less commonly seen in SG procedures vs. that in RYGB procedures.

**Conclusion**

-Histological findings were significant for parietal cell hyperplasia, deeper mucosal glands, muscular hypertrophy, and chronic gastritis in an SG gastric biopsy.

-Parietal cells were noted around the neck of the mucosal glands in only the gastric fundus and body.

-Without the intact stomach’s ability to not only regenerate parietal cells, but also increase its number in the gastric body of an SG patient, SG is a better alternative to RYGB in terms of limiting Vitamin B12 Deficiency.

**References**