

INTRODUCTION

- 1.6 billion people worldwide are obese with 2.5 million deaths annually
- Healthcare spending in the United States for obesity has surpassed \$100 billion annually
- 228,000 bariatric surgeries were performed in the United States in 2017
- 20-50% of patients undergoing bariatric surgery in the United States have a history of a mood disorder
- Studies have shown as high as 35% of bariatric surgery candidates were taking antidepressants
- Unlike medications for diabetes, hypertension, or hyperlipidemia, which are usually discontinued post bariatric surgery, antidepressant medication use has been found to only decrease by 9% one year after bariatric surgery

OBJECTIVES

- Describe a case of major depressive disorder in a patient with history of roux-en-y gastric (RYGB) procedure
- Briefly review types of bariatric surgeries
- Review the literature for antidepressant efficacy in patients status post bariatric surgery, with focus on selective serotonin reuptake inhibitors (SSRI) and serotonin-norepinephrine reuptake inhibitors (SNRI)
- Review the evidence for transitioning to immediate release formulations when available

CASE

- 62 year old female with history of MDD and GAD who was status post RYGB with past medical history significant for hypertension, fibromyalgia, irritable bowel syndrome and migraines
- Presented to outpatient psychiatry residency clinic with worsening depression and anxiety.
- Medications included duloxetine 60mg daily, bupropion XL 300mg daily, clonazepam 1mg nightly and 0.5mg daily PRN anxiety, topiramate 50mg daily, tramadol 50mg daily PRN pain, pantoprazole 20mg BID, estradiol 1mg daily.
- Initial concern for decreased absorption of duloxetine given history of RYGB but quick literature search revealed limited data. We elected to increase duloxetine to 90mg daily. Bupropion XL was continued due to lack of evidence for switching to IR or SR formulations.
- Follow up 4 weeks later revealed improvement in depression and anxiety symptoms. Further follow up has continued to reveal improved symptoms of depression and anxiety since increase in duloxetine, furthering our hypothesis that absorption of duloxetine was poor.

DISCUSSION

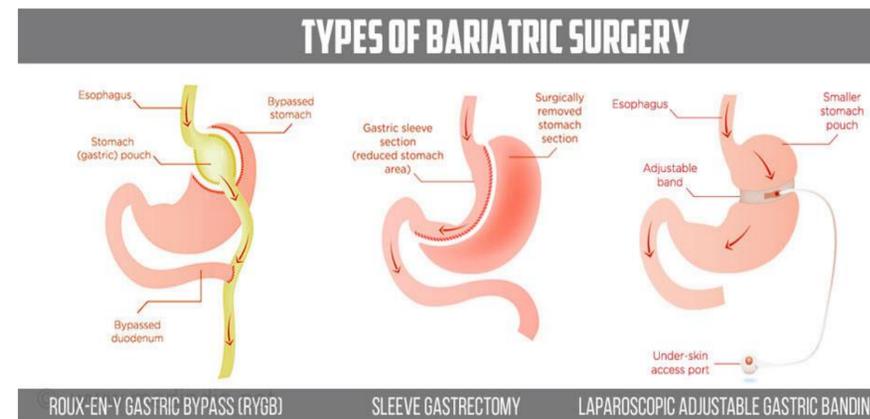


Table 1: 2015-2017 percentage estimates of bariatric surgery (ASMBS)
(data from ASMBS published 2018)

	2015	2016	2017
Sleeve	53.61%	58.11%	59.39%
RYGB	23.02%	18.69%	17.80%
Gastric Band	3.39%	3.39%	2.77%

Table 2: Effects of bariatric surgery on mechanisms of absorption of oral medications

Effect	RYGB	Gastric Band	Sleeve Gastrectomy
Reduced gastric acidity	X		X
Diminished intestinal surface area	X		
Gastric emptying	X	X	X
Gastric motility	X	X	X
Rapid Weight loss (V_d)	X	X	X
Changes in CYP450 system (3A4 and 3A5 found in upper SI)	X		
Malabsorption of various vitamins and minerals that function as enzymatic co-factors of various neurotransmitters	X		

Table 3: Summary of available literature on antidepressant bioavailability after bariatric surgery

Study	Medications	Results
Hamad et al.	Multiple Medications	8/12 showed that AUC dropped an average of 54% at 1 month
Marzinke et al.	escitalopram	33% reduction at 2 weeks and further 16-19% reduction at 6 weeks
Roerig et al.	sertraline	Levels were lower post surgery (bariatric 124.4 ng hour/mL versus control 314.8ng hour/mL)
Roerig et al.	duloxetine	Levels were lower post surgery (bariatric 646.74 ng hour/mL versus control 1119.91 ng hour/mL)
Krieger et al.	venlafaxine XR	AUC was similar before and after surgery

- Literature review was conducted through PubMed and EMBASE using the terms “bariatric surgery”, “gastric bypass”, “SSRI”, “SNRI”, “antidepressants”, and “anti-depressants”
- There were 11 publications that looked at antidepressant use after bariatric surgery. The majority of publications focused on antidepressant use (mainly SSRI and SNRI) after RYGB
- Though majority of research to date is on RYGB procedure, current trends in bariatric surgery show that the most common procedure in 2017 was sleeve gastrectomy, with 59.39% of procedures using this technique. (Figure 1 & Table 1)
- Each procedure type (RYGB, gastric band, sleeve gastrectomy) affects various mechanisms of both pharmacokinetics and pharmacodynamics of medications. Table 2 references the effects that each of the three most common bariatric surgery techniques have on various mechanisms of absorption
- Research is limited on specific antidepressants but Table 3 highlights the data found for common SSRI and SNRIs
- Literature review found that diabetic and cardiovascular agents are reduced, but antidepressants remain constant or increase, with some studies showing a 1.13 fold increase in antidepressant use post bariatric surgery. One study looking at antidepressant use after bariatric surgery found 40% had no change, 23% increased the dose, 18% changed to a different antidepressant, and 16% decreased or stopped antidepressant
- Other studies revealed that those with co-morbid psychiatric diagnoses lose significantly less weight and death rates for non-disease related deaths (accidents and suicides) were found to be increased by a factor of 1.58 compared to controls
- Many disadvantages of using an immediate release (IR) oral drug after bariatric surgery were discussed including negative impact on disintegration of drug products, decreased amount of fluid in stomach to act as solvent, and change in gastric pH

CONCLUSIONS

- Despite the increase in bariatric surgeries, there are no specific guidelines for treatment of psychiatric patients post surgery
- Given the documented link between obesity and psychiatric disorders, close follow up by a psychiatric provider would likely be beneficial for patients, especially those currently on antidepressant medications
- Each type of bariatric surgery presents different effects on the metabolism of antidepressants and thus requires considerations about bioavailability and its impact on side effect profiles, especially antidepressants with high propensity for discontinuation syndromes
- Most of the literature to date is based off of RYGB, but there has been a decrease in RYGB and increase in both gastric sleeve and gastric band; therefore further studies are needed
- Some recommendations include use of liquid formulations for at least 2 months and crushing or opening up pills, if possible, to help with bioavailability
- Though a common clinical practice, there is no clear evidence to support switching from extended release formulations to immediate release following bariatric surgery
- Patients undergoing bariatric surgery are at increased risk for depression and suicide, so close follow up by psychiatry for at least a one year period would be beneficial
- Therapeutic drug monitoring could play an important role moving forward, specifically in the first month to 12 months after bariatric surgery
- In summary, further research of psychiatric patients status post bariatric surgery is needed to determine guidelines for treatment**

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