# REVIEW

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# Drug absorption in bariatric surgery patients: A narrative review

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#### Abstract

Background: Despite the increase in the number of bariatric surgeries performed, little is known about the impact of the surgery on drug absorption. Unpredictability is assumed with drugs, given the anatomical changes after surgery.

Objective: To evaluate the impact of bariatric surgery on drug absorption based on the type of procedure performed.

Methods: We conducted a comprehensive literature review searching PubMed/ Medline for published studies (from inception to December 2017) that evaluate the use of drugs and the assessment of drug absorption after bariatric surgery. Pharmacokinetic/pharmacodynamic studies, case reports, and observational studies were included in our review.

**Results:** We found 60 studies addressing drug use after bariatric surgery. Twentyeight studies reported a decrease in drug absorption after bariatric surgery while only four studies showed an increase in drug absorption. Unchanged absorption of drugs was seen in 23 studies after the surgery.

**Conclusion:** The available information shows variations in drug absorption after bariatric surgery. The unpredictability may result from factors related to the patient, drug, and/or type of surgery. Therefore, pharmacists' involvement and close monitoring of patients after bariatric surgery could be effective to avoid sub-/ supratherapeutic responses.

#### KEYWORDS

bariatric surgery, drug absorption, drug use, pharmacotherapy, therapeutics

# **1** | BARIATRIC SURGERY

Recent years have seen increases in the utilization of bariatric surgery, often known as obesity surgery, metabolic surgery, or weight loss surgery.<sup>1</sup> Bariatric surgery has been attributed to long-term weight loss, which is rarely achieved using pharmacological

treatments and lifestyle modification approaches. Studies show that bariatric surgery is more effective than pharmacological, lifestyle, and dietary interventions and can significantly improve comorbidities such as diabetes, sleep apnea, hypertension, and hyperlipidemia.<sup>2,3</sup> Obese patients who undergo bariatric surgery are more likely to have comorbidities that require pharmacotherapy management.

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The pharmacokinetic and pharmacodynamic properties of medications used in comorbidities management can be affected by the changes resulting from bariatric surgery. These changes in pharmacokinetic and pharmacodynamic properties are primarily due to the anatomical alterations caused by bariatric procedures, which are restrictive, malabsorptive, or a combination of restrictive and malabsorptive.<sup>4</sup> Restrictive procedures aim to decrease the amount of food ingested, as used in sleeve gastrectomy (SG), vertical banded gastroplasty (VBG), adjustable gastric banding (AGB), and gastric stapling. Malabsorptive procedures reduce the absorption of nutrients from food, such as in jejunoileal bypass (JIB) and jejunocolic bypass. Other bariatric procedures combine restrictive and malabsorptive techniques to achieve less food volume ingestion and less absorption of nutrients. These techniques are used in Roux-en-Y gastric bypass (RYGB), distal gastric bypass, duodenal switch, and biliopancreatic diversion with duodenal switch (BPD-DS).<sup>4,5</sup> Consequently, most drugs are expected to behave differently in a bariatric population compared to a non-bariatric population.

In recent years, SG and RYGB were the most performed procedures compared to other procedures, such as JIB, VBG, AGB, and BPD-DS. In SG, a longitudinal resection is performed to create a sleeve-like structure of the stomach along the lesser curvature. Weight loss in SG is achieved by reducing the amount of food intake, restricting caloric intake, and promoting a sensation of satiety; however, the endocrine mechanisms and related changes after SG remain unclear.<sup>6</sup> The other procedure discussed in this study is RYGB, which involves partial resection of the stomach to create a small pouch to limit the amount of food intake. This gastric pouch is stapled and anastomosed between the pouch and jejunum to disrupt the absorption of nutrients and restrict the amount of food ingested.<sup>7,8</sup> These anatomical changes may also interfere with drugs absorption, metabolism, and excretion.

## 2 | METHODS

PubMed/Medline comprehensive literature search for published studies (from inception to December 2017) was conducted. We used combinations of the following terms "drug absorption," "bariatric surgery," "gastric bypass," "bypass," "gastroplasty," "gastrectomy," "gastric banding," "sleeve gastrectomy," "malabsorption," "drug use," pharmacodynamic," and "pharmacokinetic." We included pharmacokinetic/pharmacodynamic studies, case reports, and observational studies in our review. We excluded results from non-English and animal studies.

# 3 | DRUG ABSORPTION AFTER BARIATRIC SURGERY

There is a paucity of literature that discusses the changes in pharmacokinetics and pharmacodynamics after bariatric surgery. Because obese patients are likely to use one or more medications to treat obesity-related comorbidities or to control postsurgery pain and adverse effects, it is important to understand drug absorption after bariatric surgery. Available evidence shows that drug absorption is more likely to decrease after bariatric surgery; however, the change in absorption is drug-specific and substantially affected by the type of procedure received.<sup>9,10</sup> The decrease in absorption can be due to gastric restriction caused by the surgery where the stomach surface area is significantly reduced, which decreases the amount of hydrochloric acid secreted and increases the gastric pH, leading to poor disintegration, dissolution, and absorption of acid-soluble drugs. Similarly, bariatric procedures that involve resection or bypass of the absorptive areas of the duodenum and proximal jejunum affect the dissolution and absorption of drugs due to a decrease in the surface areas for intestinal absorption. A long section of the intestines is bypassed in some bariatric procedures; thus, transporters that function as carriers of drug particles across the intestine lumen to the circulation lead to low bioavailability of drugs. Furthermore, extended-release dosage forms are designed to travel through the gastrointestinal tract to achieve adequate dissolution and absorption. The bypassing of portions of the gastrointestinal system gives the drug an insufficient transit time to reach full absorption and consequently limits the bioavailability of the administered dose.<sup>11</sup> Other drugs, such as lipophilic drugs (i.e., phenytoin, selective serotonin receptors inhibitors, and thyroxin) depend on bile acids, which function as surfactants to enhance the solubility of the drug molecules. The secretion of the bile acids is impaired by the bypass procedure, which may lead to the incomplete dissolution and absorption of lipophilic drugs.<sup>12</sup> On the other hand, other studies reported an increase in drug absorption which can be attributed to mucosal hypertrophy that causes higher absorptive capacity in the remaining part of the intestines.<sup>13</sup>

There are currently no guidelines for how to address drug use after bariatric surgery. Available studies presumed that the alterations in the gastrointestinal system after bariatric surgery are more likely to change drug absorption compared to the non-bariatric population. Patient medication counseling should be provided before hospital discharge to ensure that patients are aware of the change in drug absorption after the surgery. Close monitoring of the patients' use of drugs soon after bariatric surgery is recommended to avoid adverse effects. If the levels of the drug administered can be obtained via laboratory tests, it is recommended to monitor the drug levels frequently. Due to the impairment of disintegration and dissolution after bariatric surgery, liquid dosage forms are preferred over solid dosage forms, if available. Additionally, enteric-coated, film-coated, delayed-release, or extended-release tablets are not recommended, and immediate-release, crushable, or chewable tablets may have fewer variations in absorption after bariatric surgery. A nonoral route of administration, such as intravenous, intramuscular, subcutaneous, vaginal, rectal, or nasal dosage forms, is preferred to avoid unpredictable absorption. A limited number of studies have examined the changes in drug absorption after bariatric surgery. The available literature that assessed the absorption of drugs reported either an increased, decreased, or unchanged absorption after bariatric surgery (Table 1). Due to insufficient data, absorption is concluded to be influenced by many factors; it is "patient-specific" and "procedurespecific," and each patient should be managed independently.<sup>9</sup>

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# TABLE 1 Summary of the changes in drug absorption after bariatric surgery

Drug	Route (dosage form)	Procedure	Outcome	Comments
Amoxicillin	Oral (unspecified)	RYGB	Ineffective	A case report of a 29-year-old pregnant woman treated with amoxicillin as well as other orally administered antibiotics. Oral treatment regimens failed, which could be due to interrupted absorption. IV ceftriaxone was used to treat the infection. <sup>17</sup>
Amoxicillin/ clavulanate	Oral (unspecified)	RYGB	Ineffective	A case report of a 29-year-old pregnant woman treated with amoxicillin/ clavulanate as well as other orally administered antibiotics. Oral treatment regimens failed, which could be due to interrupted absorption. IV ceftriaxone was used to treat the infection. <sup>17</sup>
Acetaminophen	Oral (tablet)	JIB	Unchanged	A pharmacokinetic study on 8 bariatric and 15 non-bariatric patients; pre- and postsurgery. $C_{\rm max}$ and AUC were similar pre- and postsurgery. <sup>18</sup>
Acetaminophen and caffeine	Oral (unspecified)	SG RYGB	Unchanged	A controlled cohort study compared 24 patients who underwent bariatric surgery and 28 non-bariatric normal-weight patients. A lower AUC and $C_{max}$ in morbidly obese compared to healthy non-bariatric patients and bariatric patients. The bioavailability was normalized after bariatric surgery and showed no difference between bariatric surgery patients and normal weight patients. <sup>19</sup>
Ampicillin	Oral (unspecified)	JIB	Decreased	A pharmacokinetic study on 6 patients. Ampicillin was given as prodrug pivampicillin and pre- and postsurgery ampicillin levels were obtained. Bioavailability decreased significantly. <sup>20</sup>
Atorvastatin	Oral (unspecified)	RYGB	Varied	A pharmacokinetic study on 12 patients pre- and postsurgery. AUC showed both a threefold increase and twofold decrease pre- and postsurgery. <sup>21</sup>
Atorvastatin	Oral (unspecified)	BPD	Increased	A pharmacokinetic study on 10 patients pre- and postsurgery. AUC showed a twofold increase in both pre-and postoperation levels. <sup>22</sup>
Atorvastatin	Oral (unspecified)	RYGB and BPD	Decreased	A pharmacokinetic study on 12 RYGB and 10 BPD patients assessed pre- and postsurgery. The long-term effect (27 months) showed a decrease in the AUC. $^{23}$
Azithromycin	Oral (tablet)	RYGB	Decreased	A pharmacokinetic study on 14 bariatric and 14 non-bariatric patients. The AUC was 33% lower in the treatment group. $^{\rm 24}$
Caffeine	Oral (powder)	RYGB	Unchanged	A pharmacokinetic study on 18 bariatric and 18 non-bariatric patients. $C_{max}$ and AUC did not change; however, $T_{max}$ was shorter in the RYGB patients. <sup>25</sup>
Citalopram	Oral (unspecified)	RYGB	Decreased	A pharmacokinetic study on 12 bariatric patients who received SRIs. Two patients were given citalopram and showed a decrease in the AUC 1 month after surgery; however, the AUC tended to normalize 6 months after surgery. <sup>26</sup>
Cyclosporine	Oral (unspecified)	ΊΒ	Decreased	A pharmacokinetic study compared one bariatric patient to seven non- bariatric patients and showed a 50% lower concentration of cyclosporin in the bariatric patient. <sup>27</sup>
Cyclosporine	Oral (unspecified)	LAGB	Unchanged	A case report of a patient using cyclosporine after a heart transplant. Cyclosporine levels remained steady after the surgery. <sup>28</sup>
Dabigatran	Oral (capsule)	RYGB	Decreased	A case report of a 66-year-old male patient who showed a left ventricular systolic dysfunction on transesophageal echocardiogram and abnormal findings on magnetic resonance imaging alongside other thromboembolic symptoms. The study indicated that anticoagulation with dabigatran was subtherapeutic. Later, the patient's symptoms were improved after bridged with heparin and switched to warfarin. <sup>29</sup>
Dabigatran	Oral (capsule)	RYGB	Decreased	A case report of a 67-year-old female patient who showed subtherapeutic serum trough levels of dabigatran. The patient was switched to warfarin to evade thromboembolic events. <sup>29</sup>

(Continues)

# TABLE 1 (Continued)

Drug	Route (dosage form)	Procedure	Outcome	Comments
Dextromethorphan	Oral (syrup)	RYGB	Unchanged	A pharmacokinetic study on 18 bariatric and 18 non-bariatric patients. $C_{max}$ and AUC did not change; however, $T_{max}$ was shorter in the RYGB patients. <sup>25</sup>
Digoxin	Oral (tablet)	RYGB	Unchanged	A pharmacokinetic study on 12 bariatric patients pre- and postsurgery. $T_{\rm max}$ was lower in the RYGB patients. However, the AUC did not change. <sup>30</sup>
Digoxin	Oral (tablet)	JIB	Unchanged	A pharmacokinetic study on 7 patients pre- and postsurgery. The AUC remained unchanged. $^{\rm 31}$
Duloxetine	Oral (unspecified)	RYGB	Decreased	A pharmacokinetic study on 12 bariatric patients who received SRIs. One patient was given duloxetine and showed a decrease in AUC 1 month after surgery; however, the AUC tended to normalize at 6 months after surgery. <sup>26</sup>
Duloxetine	Oral (tablet)	RYGB	Decreased	A case control Pharmacokinetic study on 10 bariatric and non-bariatric patients. Bariatric patients were exposed to 57% of the drug compared to non-bariatric patients. AUC and $T_{max}$ were lower, while $C_{max}$ did not change. <sup>32</sup>
Escitalopram	Oral (unspecified)	RYGB	Decreased	A pharmacokinetic study on 12 bariatric patients who received SRIs. Two patients were given escitalopram and showed a decrease in the AUC 1 month after surgery; however, the AUC began to normalize at 6 months after surgery. <sup>26</sup>
Escitalopram	Oral (unspecified)	RYGB	Decreased	A pharmacokinetic study on four patients pre- and postsurgery. Bioavailability decreased after the surgery. <sup>33</sup>
Ethosuximide	Oral (unspecified)	JIB	Decreased	A case report of a patient who underwent JIB surgery and showed a decrease in ethosuximide absorption; therefore, a dose increase was warranted. $^{\rm 34}$
Furosemide	Oral (tablet)	RYGB	Unchanged	A pharmacokinetic study on 18 bariatric and 18 non-bariatric patients. The $C_{max}$ and AUC did not change; however, $T_{max}$ was shorter in the RYGB patients. <sup>25</sup>
Hydrochlorothiazide	Oral (unspecified)	JIB	Decreased	A pharmacokinetic study of five patients showed a 50% lower AUC in bariatric users compared to healthy users. $^{\rm 35}$
Imatinib	Oral (unspecified)	SG	Decreased	A case report of a patient who has been treated with imatinib and had achieved therapeutic plasma concentration levels before bariatric surgery. After bariatric surgery, the patient had lower $C_{\rm max}$ and AUC levels. The plasma concentration was 60% lower after the surgery. <sup>36</sup>
Lamotrigine	Oral (unspecified)	RYGB	Unchanged	A case report of a patient who was diagnosed with epilepsy and treated with phenytoin plus phenobarbital. The levels of these two drugs became subtherapeutic following surgery. Phenytoin was replaced by lamotrigine, which showed therapeutic levels. <sup>37</sup>
Levothyroxine	Oral (tablet)	RYGB	Unchanged	A pharmacokinetic study on 15 bariatric and 15 non-bariatric patients. AUC of the total T4, free T4, and $\Delta$ TSH had the same levels in both groups. <sup>36</sup>
Levothyroxine	Oral (tablet)	RYGB	Decreased	A case series of 4 patients who were treated with levothyroxine tablets showed supra-therapeutic TSH levels after the surgery compared to the levels before the surgery. The patients were switched to levothyroxine oral solution; the TSH levels were then in the normal range. <sup>39</sup>
Linezolid	Oral (unspecified) and IV	RYGB	Increased	A pharmacokinetic crossover pre- and postsurgery study. AUC increased and clearance was decreased after the surgery, suggesting lower doses after bariatric surgery. <sup>40</sup>
Metformin	Oral (tablet)	RYGB	Increased	A pharmacokinetic trial of 16 bariatric and 16 non-bariatric patients matched based on BMI and gender. The bariatric group showed 50% higher bioavailability and 21% higher AUC. <sup>41</sup>
Methylphenidate	Oral (tablet immediate	RYGB	Ineffective	A case report of an ADHD adult patient who reported a lack of efficacy after RYGB. Switching an immediate-release tablet to a slow-release

### TABLE 1 (Continued)

Drug	Route (dosage form)	Procedure	Outcome	Comments
	release/slow- release)			tablet did not improve the efficacy. A therapeutic effect was obtained after switching to the transdermal dosage form. $^{\rm 42}$
Midazolam	Oral (unspecified) and IV	RYGB	Unchanged	A pharmacokinetic study on 18 bariatric and 18 non-bariatric patients. $C_{\max}$ did not change; however, there was a slightly lower AUC and shorter $T_{\max}$ in the RYGB patients. <sup>25</sup>
Midazolam	Oral (tablets) IV (vial)	RYGB	Unchanged	A pharmacokinetic study on 18 patients pre- and postsurgery. Bioavailability remained unchanged, although systematic clearance increased by 1.7-fold. <sup>43</sup>
Midazolam	Oral (solution)	RYGB	Unchanged	A pharmacokinetic study on 12 bariatric patients; pre-and postsurgery. $T_{\rm max}$ was lower in the RYGB patients. However, the AUC did not change. <sup>30</sup>
Moxifloxacin	Oral (tablet) and IV	RYGB	Increased	A pharmacokinetic crossover study on 12 patients who showed higher $C_{\rm max}$ and AUC after bariatric surgery. $^{44}$
Mycophenolic acid	Oral (unspecified)	RYGB	Decreased	A pharmacokinetic study compared the levels of six bariatric patients to the levels of published levels of non-bariatric patients. The AUC was significantly lower in the bariatric patients. <sup>45</sup>
Nitrofurantoin	Oral (unspecified)	RYGB	Ineffective	A case report of a 29-year-old pregnant woman treated with nitrofurantoin among other orally administered antibiotics. Oral treatment regimens failed, which could be due to interrupted absorption. IV ceftriaxone was used to treat the infection. <sup>17</sup>
Omeprazole	Oral (unspecified)	RYGB	Unchanged	A pharmacokinetic study on 18 bariatric and 18 non-bariatric patients. $C_{max}$ and the AUC did not change; however, $T_{max}$ was shorter in the RYGB patients. <sup>25</sup>
Penicillin V	Oral (tablet)	JIB	Increased	A pharmacokinetic study on eight bariatric patients; pre-and postsurgery. $C_{\rm max}$ and AUC were higher after surgery. <sup>18</sup>
Oral contraceptives	Oral (unspecified)	BPD	Decreased	A prospective pre- and postsurgery study using a questionnaire of 40 women. The study concluded that an oral contraceptive may fail when used in bariatric patients due to a lack of absorption. <sup>46</sup>
Oral contraceptives	Oral (unspecified)	JIB	Unchanged	A pharmacokinetic study on 12 bariatric and 6 non-bariatric patients to compare absorption in both groups. The plasma concentration of the drugs was similar between the groups. <sup>47</sup>
Oral contraceptives	Oral (unspecified)	JIB	Decreased	A pharmacokinetic study on six bariatric and five non-bariatric patients concluded that the AUC was lower in bariatric patients. <sup>48</sup>
Phenytoin	Oral (unspecified)	RYGB	Decreased	A case report of a patient who was diagnosed with epilepsy and treated with phenytoin plus phenobarbital and never had an episode for 30 years. The patient had an episode 1 year after the surgery; phenytoin levels were subtherapeutic. <sup>37</sup>
Phenytoin	Oral (capsule)	JIB	Decreased	A pharmacokinetic study on seven bariatric and nine non-bariatric patients. Absorption and AUC were lower in the bariatric group. $^{49}$
Phenytoin	Oral (unspecified)	JIB	Decreased	A case report of a patient who underwent JIB reversal surgery and showed a decrease in phenytoin absorption and was recommended to increase the dose. $^{50}$
Phenytoin	Oral (unspecified)	JIB	Decreased	A case report of a patient who underwent JIB surgery showed a decrease in phenytoin absorption; therefore, a dose increase was warranted. $^{\rm 34}$
Phenobarbital	Oral (unspecified)	RGYB	Decreased	A case report of a patient who was diagnosed with epilepsy and treated with phenytoin plus phenobarbital and never had an episode for 30 years. The patient had an episode 1 year after the surgery, and phenobarbital levels were subtherapeutic. <sup>37</sup>
Propylthiouracil	Oral and IV	JIB	Unchanged	A pharmacokinetic study on nine patients; pre- and postsurgery. Drug levels were obtained, and approximately 80% of the drug bioavailability did not change. <sup>20</sup>

6 of 8 WILEY\_Health Science Reports

#### TABLE 1 (Continued)

Drug	Route (dosage form)	Procedure	Outcome	Comments
Ranitidine	Oral (tablet)	BPD	Unchanged	A pharmacokinetic study on seven patients who underwent bariatric surgery showed AUC and plasma concentrations similar to those in non-bariatric patients. <sup>51</sup>
Ranitidine	Oral (tablet)	BPD	Unchanged	A pharmacokinetic study on 10 patients pre- and postsurgery and 11 patients who did not go through the surgery. Drug levels were obtained; $C_{max}$ and AUC were similar among the presurgery, postsurgery, and normal patients. <sup>52</sup>
Rivaroxaban	Oral (tablet)	RYGB	Unchanged	A case report of a patient who was unstable on warfarin anticoagulation treatment. The patient was switched to rivaroxaban and showed normal absorption of rivaroxaban. <sup>53</sup>
Sertraline	Oral (unspecified)	RYGB	Decreased	A pharmacokinetic study on 12 bariatric patients who received SRIs. Two patients were given sertraline and showed a decrease in the AUC 1 month after the surgery; however, the AUC tended to normalize 6 months after the surgery. <sup>26</sup>
Sirolimus	Oral (tablet)	RYGB	Decreased	A pharmacokinetic study compared the levels of six bariatric patients to published levels of non-bariatric patients. The AUC was significantly lower in the bariatric patients. <sup>45</sup>
Tacrolimus	Oral (unspecified)	RYGB	Decreased	A pharmacokinetic study compared the levels of six bariatric patients to the published levels of non-bariatric patients. The AUC was significantly lower in the bariatric patients. <sup>45</sup>
Tamoxifen	Oral (tablet)	RYGB	Decreased	A case series of three women who showed subtherapeutic levels after surgery. $^{\rm 54}$
Temozolomide	Oral (unspecified)	RYGB	Unchanged	A case report of one patient who showed no changes in $C_{max}$ or AUC compared to the data of non-bariatric patients. <sup>55</sup>
Tolbutamide	Oral (tablet)	RYGB	Unchanged	A pharmacokinetic study on 18 bariatric and 18 non-bariatric patients. $C_{max}$ and AUC did not change; however, $T_{max}$ was shorter in the RYGB patients. <sup>25</sup>
Venlafaxine	Oral (unspecified)	RYGB	Decreased	A pharmacokinetic study on 12 bariatric patients who received SRIs. Five patients were given venlafaxine and showed a decrease in AUC 1 month after the surgery; however, the AUC tended to be normalized 6 months after the surgery. <sup>26</sup>
Warfarin	Oral (tablet)	RYGB and gas- trectomy	Resistance	A case report of a patient who developed warfarin resistance after bariatric surgery despite a dose increase. $^{56}$
Warfarin	Oral (tablet)	RYGB	Unchanged	A small cohort study matched 27 bariatric surgery patients to 59 non- bariatric surgery patients to assess warfarin dose change. Bariatric surgery patients showed a continuous decrease in warfarin doses following the surgery compared to non-bariatric patients. However, the doses returned to those used in non-bariatric surgery patients. The change in INR values did not parallel the change in warfarin doses. <sup>57</sup>

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; AUC, area under the curve; BMI, body mass index; BPD, biliopancreatic diversion;  $C_{max}$ , maximum serum concentration; INR, international normalized ratio; IV, intravenous; JIB, jejunoileal bypass; LABG Laparoscopic adjustable gastric banding; RYGB Roux-en-Y gastric bypass; SG sleeve gasterectomy; SRI, serotonin reuptake inhibitor; T4, thyroxin;  $T_{max}$ , time to maximum concentration; TSH, thyroid-stimulation hormone.

Collaborations between pharmacists and surgeons can improve perioperative bariatric surgery patients' pharmaceuticals. Additionally, due to the possible changes in drug absorption and the expected need for drug adjustment, pharmacists' involvement in the drug management and drug reconciliation upon discharge can ensure a safe and effective transition for bariatric surgery patients.<sup>14–16</sup>

# 4 | CONCLUSION

Drug absorption shows variations after bariatric surgery. The available data ascribed the variations in absorption to many factors including route of administration, dosage form, patient-specific factors, type of surgery, and pharmacokinetic/pharmacodynamic considerations. Therefore, patient-tailored therapy with close monitoring of drugs is warranted after bariatric surgery. Prescribing and dosing guidelines alongside the engagement of specialized healthcare professionals such as pharmacists may help improve therapeutic outcomes in this patient population. Further studies to evaluate the use of drugs in the bariatric surgery population are needed.

#### AUTHOR CONTRIBUTIONS

Abdullah A. Alalwan, Jeffrey Friedman, and Abraham Hartzema: Conceptualization. Abdullah A. Alalwan: Formal analysis. Abdullah A. Alalwan, Osamah Alfayez, Jeffrey Friedman, and Abraham Hartzema: Writing – review and editing. Abdullah A. Alalwan: Writing – original draft. Dr. Abdullah A. Alalwan had full access to all the studies in this review.

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#### CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

#### TRANSPARENCY STATEMENT

We confirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

#### DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article (and/or) its supplementary materials.

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#### REFERENCES

- Alalwan AA, Friedman J, Park H, Segal R, Brumback BA, Hartzema AG. US national trends in bariatric surgery: a decade of study. Surgery. 2021;170(1):13-17.
- Mechanick JI, Youdim A, Jones DB, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient—2013 update: cosponsored by American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery. *Obesity*. 2013;21:S1-S27.
- O'Brien PE, Dixon JB, Laurie C, et al. Treatment of mild to moderate obesity with laparoscopic adjustable gastric banding or an intensive medical program. Ann Intern Med. 2006;144(9):625.
- Geraldo M, Feder D, Affonso Fonseca FL, de Fatima Veiga Gouveia MR
   The use of drugs in patients who have undergone bariatric surgery. *Int J Gen Med.* 2014;7:219-224.
- Abeles D, Shikora S. Bariatric surgery: current concepts and future directions. *Aesthetic Surg J.* 2008;28(1):79-84.

6. Rosenthal RJ. International sleeve gastrectomy expert panel consensus statement: best practice guidelines based on experience of >12,000 cases. *Surg Obes Relat Dis.* 2012;8(1):8-19.

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- Higa KD. Laparoscopic Roux-en-Y gastric bypass for morbid obesity. Arch Surg. 2000;135(9):1029-1033.
- Matthews BD, Sing RF, DeLegge MH, Ponsky JL, Heniford BT. Initial results with a stapled gastrojejunostomy for the laparoscopic isolated Roux-en-Y gastric bypass. *Am J Surg.* 2000;179(6):476-481.
- Padwal R, Brocks D, Sharma A. A systematic review of drug absorption following bariatric surgery and its theoretical implications. *Obesity*. 2010;11(1):41-50.
- Azran C, Wolk O, Zur M, et al. Oral drug therapy following bariatric surgery: an overview of fundamentals, literature and clinical recommendations. *Obes Rev.* 2016;17(11):1050-1066.
- 11. Miller AD. Medication and nutrient administration considerations after bariatric surgery. *Am J Heal Pharm.* 2006;63(19):1852-1857.
- 12. Andari Sawaya R, Jaffe J, Friedenberg L, Friedenberg KF. Vitamin, mineral, and drug absorption following bariatric surgery. *Curr Drug Metab.* 2012;13(9):1345-1355.
- 13. Padwal R, Brocks D, Sharma AM. A systematic review of drug absorption following bariatric surgery and its theoretical implications. *Obes Rev.* 2010;11(1):41-50.
- 14. Silverman JB, Catella JG, Tavakkolizadeh A, Robinson MK, Churchill WW. Bariatric surgery pharmacy consultation service. *Obes Surg.* 2011;21(9):1477-1481.
- Van Prooyen AM, Hicks JL, Lin E, et al. Evaluation of an inpatient pharmacy consult on discharge medications in bariatric surgery patients. J Pharm Pract. 2021. https://journals.sagepub.com/doi/ abs/10.1177/08971900211030238
- Falconer EA, Harris DA, Van Prooyen A, et al. Pharmacy-led initiative for improving peri-operative medication reconciliation among bariatric surgical patients: what is the role? *Surg Endosc.* 2022;36(2): 1593-1600.
- Magee SR, Shih G, Hume A. Malabsorption of oral antibiotics in pregnancy after gastric bypass surgery. J Am Board Fam Med. 2007; 20(3):310-313.
- Terry S, Gould J, McManus J, Prescott L. Absorption of penicillin and paracetamol after small intestinal bypass surgery. *Eur J Clin Pharmacol.* 1982;23:245-248.
- Goday Arno A, Farré M, Rodríguez-Morató J, et al. Pharmacokinetics in morbid obesity: influence of two bariatric surgery techniques on paracetamol and caffeine metabolism. *Obes Surg.* 2017;27(12): 3194-3201.
- Kampmann J, Klein H, Lumholtz B, Mølholm Hansen J. Ampicillin and propylthiouracil pharmacokinetics in intestinal bypass patients followed up to a year after operation. *Clin Pharmacokinet*. 1984;9: 168-176.
- 21. Skottheim IB, Stormark K, Christensen H, et al. Significantly altered systemic exposure to atorvastatin acid following gastric bypass surgery in morbidly obese patients. *Clin Pharmacol Ther.* 2009;86(3): 311-318.
- Skottheim IB, Jakobsen GS, Stormark K, et al. Significant increase in systemic exposure of atorvastatin after biliopancreatic diversion with duodenal switch. *Clin Pharmacol Ther.* 2010; 87(6):699-705.
- 23. Jakobsen GS, Skottheim IB, Sandbu R, et al. Long-term effects of gastric bypass and duodenal switch on systemic exposure of atorvastatin. *Surg Endosc.* 2013;27(6):2094-2101.
- 24. Padwal RS, Ben-Eltriki M, Wang X, et al. Effect of gastric bypass surgery on azithromycin oral bioavailability. *J Antimicrob Chemother*. 2012;67(9):2203-2206.
- Tandra S, Chalasani N, Jones D, Mattar S, Hall S, Vuppalanchi R. Pharmacokinetic and pharmacodynamic alterations in the Roux-en-Y gastric bypass recipients. *Ann Surg.* 2013;258(2):262-269.

- Hamad GG, Helsel JC, Perel JM, et al. The effect of gastric bypass on the pharmacokinetics of serotonin reuptake inhibitors. *Am J Psychiatry*. 2012;169(3):256-263.
- Chenhsu R, Wu Y, Katz D, Rayhill S. Dose-adjusted cyclosporine c2 in a patient with jejunoileal bypass as compared to seven other liver transplant recipients. *Ther Drug Monit.* 2003;25(6):665-670.
- Ablassmaier B, Klaua S, Jacobi C, Müller J. Laparoscopic gastric banding after heart transplantation. Obes Surg. 2002;12(3):412-415.
- Lee D, DeFilipp Z, Judson K, Kennedy M. Subtherapeutic anticoagulation with dabigatran following Roux-en-Y gastric bypass surgery. J Cardiol Cases. 2013;8(1):e49-e50.
- Chan LN, Lin YS, Tay-Sontheimer JC, et al. Proximal Roux-en-Y gastric bypass alters drug absorption pattern but not systemic exposure of CYP3A4 and p-glycoprotein substrates. *Pharmacother* J Hum Pharmacol Drug Ther. 2015;35(4):361-369.
- Marcus FI, Quinn EJ, Horton H, et al. The effect of jejunoileal bypass on the pharmacokinetics of digoxin in man. *Circulation*. 1977;55(3): 537-541.
- Roerig J, Steffen K, Zimmerman C, Mitchell J, Crosby R, Cao L. Preliminary comparison of sertraline levels in postbariatric surgery patients versus matched nonsurgical cohort. *Surg Obes Relat Dis.* 2012;8(1):62-66.
- Marzinke MA, Petrides AK, Steele K, et al. Decreased escitalopram concentrations post Roux-en-Y gastric bypass surgery. *Ther Drug Monit.* 2015;37(3):408-412.
- Peterson D, Zweig R. Absorption of anticonvulsants after jejunoileal bypass. Bull Los Angeles Neurol Soc. 1974;39(2):51-55.
- Backman L, Beerman B, Groschinsky-Grind M, Hallberg D. Malabsorption of hydrochlorothiazide following intestinal shunt surgery. *Clin Pharmacokinet*. 1979;4(1):63-68.
- Pavlovsky C, Egorin M, Shah D, Beumer J, Rogel S, Pavlovsky S. Imatinib mesylate pharmacokinetics before and after sleeve gastrectomy in a morbidly obese patient with chronic myeloid leukemia. *Pharmacotherapy*. 2009;29(9):1152-1156.
- Pournaras D, Footitt D, Mahon D, Welbourn R. Reduced phenytoin levels in an epileptic patient following Roux-En-Y gastric bypass for obesity. Obes Surg. 2011;21(5):684-685.
- Rubio I, Galrão A, Santo M, Zanini A, Medeiros-Neto G. Levothyroxine absorption in morbidly obese patients before and after Roux-En-Y gastric bypass (RYGB) surgery. Obes Surg. 2012;22(2):253-258.
- Pirola I, Formenti AM, Gandossi E, et al. Oral liquid I-thyroxine (I-T4) may be better absorbed compared to I-T4 tablets following bariatric surgery. Obes Surg. 2013;23(9):1493-1496.
- Hamilton R, Thai X, Ameri D, Pai M. Oral bioavailability of linezolid before and after Roux-en-Y gastric bypass surgery: is dose modification necessary in obese subjects? J Antimicrob Chemother. 2013;68(3):666-673.
- Padwal RS, Gabr RQ, Sharma AM, et al. Effect of gastric bypass surgery on the absorption and bioavailability of metformin. *Diabetes Care.* 2011;34(6):1295-1300.
- Azran C, Langguth P, Dahan A. Impaired oral absorption of methylphenidate after Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2017;13(7):1245-1247.
- Brill MJ, van Rongen A, van Dongen EP, et al. The pharmacokinetics of the CYP3A substrate midazolam in morbidly obese patients

before and one year after bariatric surgery. *Pharm Res.* 2015;32(12): 3927-3936.

- 44. De Smet J, Colin P, De Paepe P, et al. Oral bioavailability of moxifloxacin after Roux-en-Y gastric bypass surgery. J Antimicrob Chemother. 2012;67(1):226-229.
- 45. Rogers C, Alloway R, Alexander J, Cardi M, Trofe J, Vinks A. Pharmacokinetics of mycophenolic acid, tacrolimus and sirolimus after gastric bypass surgery in end-stage renal disease and transplant patients: a pilot study. *Clin Transplant*. 2007;22(3): 281-291.
- Gerrits E, Ceulemans R, van Hee R, Hendrickx L, Totté E. Contraceptive treatment after biliopancreatic diversion needs consensus. Obes Surg. 2003;13(3):378-382.
- Andersen A, Lebech P, Sorensen T, Borggaard B. Sex hormone levels and intestinal absorption of estradiol and D-norgestrel in women following bypass surgery for morbid obesity. *Int Obes.* 1982;6(1): 91-96.
- Victor A, Odlind V, Kral J. Oral contraceptive absorption and sex hormone binding globulins in obese women: effects of jejunoileal bypass. *Gastroenterol Clin North Am.* 1987;16(3):483-491.
- 49. Kennedy M, Wade D. Phenytoin absorption in patients with ileojejunal bypass. Br J Clin Pharmacol. 1979;7(5):515-518.
- 50. Peterson D. Phenytoin absorption following jejunoileal bypass. *Bull Clin Neurosci.* 1983;48:148-149.
- Adami G, Gandolfo P, Esposito M, Scopinaro N. Orally-administered serum ranitidine concentration after biliopancreatic diversion for obesity. *Obes Surg.* 1991;1(3):293-294.
- 52. Cossu ML, Caccia S, Coppola M, et al. Orally administered ranitidine plasma concentrations before and after biliopancreatic diversion in morbidly obese patients. *Obes Surg.* 1999;9(1):36-39.
- Mahlmann A, Gehrisch S, Beyer-Westendorf J. Pharmacokinetics of rivaroxaban after bariatric surgery: a case report. J Thromb Thrombolysis. 2013;36(4):533-535.
- Wills S, Zekman R, Bestul D, Kuwajerwala N, Decker D. Tamoxifen malabsorption after Roux-en-Y gastric bypass surgery: case series and review of the literature. *Pharmacotherapy*. 2010;30(2):217.
- Park D, Shah D, Egorin M, Beumer J. Disposition of temozolomide in a patient with glioblastoma multiforme after gastric bypass surgery. J Neurooncol. 2009;93(2):279-283.
- Sobieraj DM, Wang F, Kirton OC. Warfarin resistance after total gastrectomy and Roux-en-Y esophagojejunostomy. *Pharmacotherapy*. 2008;28(12):1537-1541.
- Irwin AN, McCool KH, Delate T, Witt DM. Assessment of warfarin dosing requirements after bariatric surgery in patients requiring long-term warfarin therapy. *Pharmacotherapy*. 2013;33(11): 1175-1183.

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