Medication Use Among Patients Prior to Bariatric Surgery

Jennifer Padden Elliott, PharmD,¹ Erica L. Gray, PharmD candidate,¹
Jessie Yu, PharmD candidate,¹ and Melissa A. Kalarchian, PhD²

Purpose: The aims of this study were to describe the most common medications reported by candidates for weight loss surgery and to consider the potential implications for patient care.

Methods: A secondary data analysis of data from bariatric surgery patients enrolled in a randomized, controlled trial. At study entry, participants recorded their use of prescription medications they had taken in the previous 90 days. The Anatomical Therapeutic Chemical (ATC)/Defined Daily Dose (DDD) Index 2014 was used to classify medications.

Results: Participants ($n=265$) were 85.7% female and 83.0% white. Mean body mass index was 47.9 ± 6.5 kg/m², and age was 45.1 ± 11 years. The average number of medications was 4.4 ± 4.1 , and the median was 3. The top three anatomical main groups were the cardiovascular system, alimentary tract and metabolism, and nervous system (28.2%, 21.6%, and 21.3% of all medications, respectively). The top therapeutic subgroups were drugs used in diabetes, psychoanaleptics, and agents acting on the renin-angiotensin system (12%, 11.3%, and 8.2% of all medications, respectively).

Conclusions: Candidates for weight loss surgery report taking medications associated with obesity-related comorbidities such as diabetes, depression, and hypertension. Although many may be able to eliminate these medications, others will require close monitoring and dosage adjustment after surgery.

Introduction

THE LATEST DATA from the National Health and Nutrition Examination Survey (NHANES) indicate that 35.1% of U.S. adults were obese and 6.4% were extremely obese in 2011–2012.¹ Current guidelines for the management of overweight and obesity suggest that motivated adults who have failed behavioral and pharmacologic treatment with a body mass index (BMI) >40 kg/m² or >35 kg/m² with obesity-related comorbid conditions may be candidates for bariatric surgery.² Bariatric surgery results in an average weight loss of 20–30 pounds, maintained for up to 10 years, along with improvements in comorbid conditions.³ For example, significant decreases in cardiovascular disorders, diabetes mellitus, chronic obstructive pulmonary disease (COPD) and other respiratory conditions, and diseases of the musculoskeletal system and connective tissue were documented among 5,502 patients following bariatric surgery, with improvements sustained for up to 3 years.⁴ Given the effects of surgery on obesity-related comorbidities, it is not surprising that medication utilization for these diseases also decreases post-surgery. Cremieux *et al.* reported a significant decrease in the frequency of medication use for infections, pain, respiratory, cardiovascular, gastroenterological, lipi-

demic, and diabetic conditions.⁴ Along with decreases in medications for diabetes, hypertension, and hyperlipidemia, modest decreases in thyroid hormones, antihistamines, and antidepressants have also been reported post-bariatric surgery.⁵

In addition to the effect that post-surgery weight loss can have on medication utilization, the surgical procedure itself can affect the absorption of medications. The most common bariatric surgeries performed in the United States are gastric bypass, gastric banding, and sleeve gastrectomy.⁶ Roux-en-Y gastric bypass (RYGB) is a malabsorptive procedure that leads to a significantly modified gastrointestinal tract, affecting drug solubility, surface area for drug absorption, and ultimately the extent and rate of drug absorption. This may result in reduced or elevated plasma levels of medications and may warrant manipulation of drug route or dose to ensure therapeutic levels.⁷ There is a lack of non-bariatric clinician knowledge regarding the effect of bariatric surgery on medication absorption, and increased pharmacist involvement in the prescription process has been recommended to avoid therapeutic failure.⁸

In order for healthcare providers to play an active role in the medication management of the post-bariatric surgery patient, it is prudent to identify the most commonly used

¹Mylan School of Pharmacy; ²School of Nursing; Duquesne University, Pittsburgh, Pennsylvania.

medications in patients undergoing bariatric surgery. The objectives of the study were to describe the most frequently utilized medications in a large sample of candidates for weight loss surgery and to consider the potential implications for clinical care.

Materials and Methods

The present study is a secondary data analysis from a randomized, controlled trial. The study was approved by the University of Pittsburgh IRB, and details on the design and initial results from the study have been reported previously.⁹ Participants were at least 18 years of age and seeking surgery at a Bariatric Center of Excellence at a large, urban medical center. Exclusion criteria included: (1) intellectual disabilities or psychosis; (2) previously diagnosed genetic obesity syndrome; (3) participation in a weight management program in the 6 months prior to study enrollment; (4) uncontrolled psychiatric symptomatology sufficiently severe to require immediate treatment; (5) pregnant or lactating in the previous 6 months; (6) taking medication during the previous 6 months with a well-established association with body weight; (8) any previous weight loss surgery; (9) medical condition requiring a specialized preoperative regimen (e.g., nonambulatory individuals, chronic obstructive pulmonary disease requiring oxygen, BMI >70 kg/m² requiring a low energy liquid diet as per the center's practice algorithm); and (10) participation in a conflicting research protocol. Of 929 patients screened for the study by telephone, 435 declined to participate and 194 did not meet the inclusion criteria. Eighty-six exclusions fell under criterion #6, with the most common exclusionary medications being topiramate ($n=23$) and quetiapine ($n=18$).

Of the remaining 300 candidates for bariatric surgery who consented to participate, 265 patients self-reported their use of prescription medications on an investigator designed, standardized data collection form and were included in the present analysis. Participants recorded their use of prescription medications that they had taken in the previous 90 days. All medication names were converted to the generic medication name.

The Anatomical Therapeutic Chemical (ATC)/Defined Daily Dose (DDD) Index 2014 was used to classify medications.¹⁰ This system is utilized internationally and is recommended by the World Health Organization (WHO) for drug utilization studies. Medications were searched using the online index, and the anatomical main group as well as the therapeutic subgroups was coded. This process can be illustrated with the prescription medication Lasix: the generic name is furosemide, the anatomical main group is the cardiovascular system, and the therapeutic subgroup is diuretics.

Patients self-reported demographic information using an investigator-designed questionnaire. Height was measured using a mounted stadiometer. Body weight was measured using a digital scale (Scale-Tronix 5002, Carol Stream, IL). Participants were weighed, and their height was measured in street clothes, without shoes. BMI was calculated as weight in kilograms divided by the height in meters squared.

Results

Demographic characteristics of study participants ($n=265$) included 85.7% female, 83.0% white, 0.8% Hispanic or

Latino, 52.5% married, and 84.5% educated beyond high school. Mean BMI was 47.9 ± 6.5 kg/m², and age was 45.1 ± 11 years.

A total of 1,153 medications were utilized by 265 patients, ranging from 0 to 20 medications each. The average was 4.4 ($SD=4.1$), and the median was 3. Thirty-six patients (13.6%) reported taking no medications, 78 (29.4%) reported taking one or two, 46 (17.4%) reported three or four, 44 (16.6%) reported five or six, and 61 (23.0%) reported more than six. Table 1 shows the medications organized by anatomical main group and therapeutic subgroups for the sample. As shown in Figure 1, the top three anatomical main groups documented were the cardiovascular system, alimentary tract and metabolism, and nervous system, representing 28.2%, 21.6%, and 21.3% of all medications, respectively. The top three therapeutic subgroups were drugs used in diabetes, psychoanaleptics, and agents acting on the renin-angiotensin system, representing 12%, 11.3%, and 8.2% of all medications, respectively.

Discussion

This descriptive study sheds light on the prescription medication profile of a relatively large sample of candidates for weight loss surgery. There was considerable variability in the number of medications reported, with most patients taking multiple medications. The medications included, but were not limited to, those for the management of disease states associated with the cardiovascular system, alimentary tract and metabolism, and nervous system. This information is useful for anticipating changes in medications as patients experience rapid weight loss and improvements in obesity-related comorbidities after surgery. Moreover, bariatric surgery reduces gastric capacity, with or without malabsorption, which may affect medication pharmacokinetics and pharmacodynamics (PK/PD).

Based on our analysis of therapeutic subgroups, drugs used to treat diabetes were the most frequently reported in this pre-surgery sample. Indeed, many patients seek bariatric surgery due to obesity-related medical comorbidities, and a growing body of research suggests that bariatric surgery is associated with high rates of diabetes remission or marked improvement in glycemic control.^{11–13} In one study involving a small population of patients with type 2 diabetes who underwent RYGB or vertical sleeve gastrectomy, 79% and 83%, respectively, stayed off their diabetes medications at 8 weeks post-surgery.¹⁴ A larger study with similar results reported diabetes medication discontinuation rates of 74.7%, 80.6%, and 84.5% at 6 months, 1 year, and 2 years.¹⁵ Therefore, although medications to treat diabetes are the most commonly reported medications utilized in this population of bariatric surgery candidates, the majority of these patients may be able to discontinue these medications successfully.

The effect of surgery on the PK/PD profile of commonly used medications to treat diabetes needs to be considered for the subset of patients who will not be able to discontinue these medications. Metformin, a first-line treatment option for type 2 diabetes and a commonly reported medication among this sample of patients, is a Biopharmaceutics Classification System (BCS) class III drug with limited absorption (low permeability and high solubility).¹⁶ A decreased intestinal surface area from certain types of bariatric surgery can further limit this medication's bioavailability.¹⁷ This

TABLE 1. MEDICATIONS REPORTED BY CANDIDATES FOR WEIGHT LOSS SURGERY (N=65)

<i>Anatomical main group and therapeutic subgroup</i>	<i>n</i>	<i>% utilization within anatomical main group</i>	<i>% utilization of all medications</i>
<i>Cardiovascular system</i>	326		28.2
1. Agent acting on the renin-angiotensin system	95	29	8.2
2. Lipid modifying agents	74	23	6.4
3. Diuretics	66	20	5.7
4. Beta blocking agents	44	13	3.8
5. Calcium channel blockers	31	9	2.7
6. Antihypertensives	8	2	0.7
7. Cardiac therapy	7	2	0.6
8. Peripheral vasodilators	3	1	0.3
<i>Alimentary tract and metabolism</i>	250		21.6
1. Drugs used in diabetes	139	56	12
2. Drugs for acid-related disorders	65	26	5.6
3. Vitamins	17	7	1.5
4. Mineral supplements	15	6	1.3
5. Antidiarrheals, intestinal anti-inflammatory/ anti-infective agents	5	2	0.4
6. Drugs for functional gastrointestinal disorders	5	2	0.4
7. Drugs for constipation	4	2	0.3
<i>Nervous system</i>	246		21.3
1. Psychoanaleptics	131	53	11.3
2. Analgesics	45	18	3.9
3. Psycholeptics	36	15	3.1
4. Antiepileptics	22	9	1.9
5. Anti-Parkinson drugs	8	3	0.7
6. Other nervous system drugs	3	1	0.3
7. Anesthetics	1	<1	0.1
<i>Respiratory system</i>	85		7.4
1. Drugs for obstructive airways disease	60	71	5.2
2. Antihistamines for systemic use	20	24	1.7
3. Nasal preparations	4	5	0.3
4. Cough and cold preparations	1	1	0.1
<i>Musculoskeletal system</i>	81		7.0
1. Anti-inflammatory and antirheumatic products	58	72	5.0
2. Muscle relaxants	14	17	1.2
3. Anti-gout preparations	5	6	0.4
5. Drugs for treatment of bone diseases	2	2	0.2
6. Topical products for joint and muscular pain	2	2	0.2
<i>Systemic hormonal preparations excl. sex hormones and insulin</i>	56		4.8
1. Thyroid therapy	56	100	4.8
<i>Genito-urinary system and sex hormones</i>	39		3.4
1. Sex hormones and modulators of the genital system	29	74	2.5
2. Urologicals	7	18	0.6
3. Contraceptives for topical use	1	3	0.1
4. Drugs for urinary frequency and incontinence	1	3	0.1
5. Gynecological anti-infectives and antiseptics	1	3	0.1
<i>Blood and blood-forming organs</i>	32		2.8
1. Antithrombotic agents	22	69	1.9
2. Anti-anemic preparations	10	31	0.9
<i>Anti-infectives for systemic use</i>	17		0.7
1. Antibacterials for systemic use	17	100	1.5
<i>Dermatologicals</i>	8		0.7
1. Corticosteroids, dermatological preparations	6	67	0.5
2. Antibiotics and chemotherapeutics for dermatological use	2	22	0.2
3. Antipsoriatics	1	11	0.1
<i>Antineoplastic and immunomodulating agents</i>	7		0.6
1. Immunosuppressants	3	43	0.3
2. Endocrine therapy	2	29	0.2
3. Antineoplastic agents	1	14	0.1
4. Immunostimulants	1	14	0.1
<i>Sensory organs</i>	6		0.5
1. Ophthalmologicals	6	100	0.5

FIG. 1. Anatomical main group classifications for 1,153 medications reported by candidates for weight loss surgery (n = 265).

potential decrease in medication bioavailability, along with the effect post-surgery weight loss can have on dosage needs, requires close monitoring of blood glucose and HbA1c levels to guide dosage adjustments after surgery.

With respect to psychoanaleptics, such as psychostimulants and some antidepressants, there has been minimal research on pharmacokinetics in the context of bariatric surgery. Understanding the impact of bariatric surgery on this therapeutic subgroup is especially important considering a high lifetime prevalence of depression and other psychiatric disorders in this population,^{18–22} as well as reports suggesting increased rates of suicide after surgery.^{23,24} In an investigation of antidepressant usage after bariatric surgery following RYGB, only 40% of patients had no change in their antidepressant medication, while 23% increased their antidepressant dose or started a new antidepressant, 18% changed antidepressant medications, and 16% decreased the dose or discontinued their antidepressant.²⁵ Two small studies on the antidepressants sertraline and duloxetine found significantly smaller area under the curve (AUC) for both medications in post-bariatric surgery patients versus matched nonsurgical controls, suggesting decreased bioavailability.^{26,27} Some have suggested that extended release products may not remain in the digestive tract for a sufficient amount of time following procedures that involve a reduction in gastrointestinal tract such as RYGB, and switching to immediate release or liquid formulations may increase bioavailability.⁷ However, research is limited, and therapeutic response should be monitored carefully after surgery.

In the present report, renin-angiotensin agents were also commonly reported among candidates for bariatric surgery. This therapeutic subgroup includes angiotensin II antagonists, angiotensin-converting enzyme inhibitors, and other agents acting on the renin-angiotensin system. Bariatric surgery has been associated with improvements hypertension and reductions in antihypertensive medications.^{12,28,29} For example, Segal *et al.* reported a 51% decrease in the use of medication for hypertension at 12 months after surgery. Although a reduction in renin-angiotensin agents may be expected with postoperative weight loss, research on pharmacokinetic implications following bariatric surgery is lacking.

The data were collected in the context of a randomized, controlled trial that had several exclusion criteria, and results

may not reflect the full population of bariatric surgery patients. For example, because patients who reported taking a medication with a well-established association with body weight, such as topiramate, were excluded upon screening for the study, the proportion of patients taking medications in the therapeutic subgroup of antiepileptics may be underestimated. Additionally, we did not collect information on dosing and compliance with medications. Nonetheless, these data may represent some of the best available data to guide clinical practice and future research in this patient population.

Conclusions

There is a growing appreciation of the effects of the different types of bariatric surgery and associated postoperative weight loss on medication utilization. This careful description and classification of prescription medication use prior to surgery, along with the discussion of potential postoperative implications, will inform healthcare providers' efforts to manage common medications in the bariatric surgery patient safely and effectively. Consideration of medication pharmacokinetics may suggest possible dosage adjustments or therapeutic alternatives after surgery, and significant postoperative weight loss may lead to decreased dosage needs or medication discontinuation. Patients will benefit from close monitoring and education after operation. More research is needed on pharmacokinetic parameters pre- and post-bariatric surgery, and this investigation may inform such efforts.

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Address correspondence to:
 Melissa A. Kalarchian, PhD
 School of Nursing
 Duquesne University
 600 Forbes Avenue
 Pittsburgh, PA 15282

E-mail: kalarchianm@duq.edu