

Article

Prevalence of Drug Interaction in Severely Obese Individuals and Associated Factors: Baseline Results from a Clinical Trial

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Abstract: The prevalence of obesity is increasing worldwide and is commonly associated with comorbidities. The use of several drugs is often necessary, which leads to Potential Drug Interactions (PDI) that may increase the morbidity and mortality. This study aimed to analyze the prevalence of drug interaction and its association with socio-demographics, health status, and drug use in severely obese individuals. Baseline data from a randomized clinical trial registered at Clinicaltrial.gov (NCT02463435) were used. A total of 150 individuals aged 18–65 years with a body mass index of 35 kg/m² were included. The outcome variable was the presence of PDI, and the explanatory variables were divided into the following four levels: socio-demographic, lifestyle, health, and medication use. The prevalence of PDI was 50% ($n = 75$) (95% CI 41–58). The variables associated with drug–drug interactions in the multiple analyses were arterial hypertension (PR 1.83, 95%, CI 1.10–3.04), polypharmacy (PR 3.12, 95%, CI 2.17–4.50), and diabetes mellitus (PR 0.60, 95%, CI 0.45–0.81). The risk factors for the occurrence of drug interaction were the presence of diabetes mellitus, hypertension, and polypharmacy.

Keywords: severe obesity; drug interaction; drug utilization reviews; randomized controlled trial; pharmacoepidemiology

1. Introduction

The prevalence of obesity has increased over the years, in particular of severe obesity. The category of obesity with body mass index (BMI) ≥ 35 kg/m² [1] presented the highest increase among other categories such as overweightness and obesity [2] and was recorded in 12% of the world population in 2015 [3]. Obesity culminates with the emergence of other comorbidities [4], such as the already well-established triad of arterial hypertension (AH) [5], diabetes mellitus (DM) [6], and hypercholesterolemia [7]. In addition, these patients may still have problems related to the renal system [8], hepatic system [9], skeletal muscle [10], and respiratory system, among others [11]. In general, this leads to a decline in an individual's health, as well as an increase in expenses and consequent overloading of health systems [12,13].

Drugs are the main therapeutic tools used for the control and treatment of these morbidities [14,15]. However, if misused, these drugs can adversely affect the patients [16] and they have been involved

in many death-related incidents arising from monitoring failures, omissions to provide necessary treatments, and potential drug interactions (PDI), among others [16,17]. PDI are responsible for therapeutic failures and constitute a safety problem as they are responsible for most of the incidents related to drug use [18]. For this reason, the World Health Organization urged its signatories to join efforts to reduce deaths associated with drug misuse by 2022 [19].

Considering the importance of PDI in drug-related morbidity and mortality [20], the prevalence and risk factors for its occurrence in groups of patients with acquired immunodeficiency syndrome [21], elderly [22], and oncology [23] is well-established. However, in the obese population, especially among the severely obese, such parameters are not yet known. Pharmacoepidemiological studies involving this group of patients are more related to elucidating pharmacological aspects of obesity treatment as well as new molecules and therapeutic targets [24,25]. A study designed to estimate the prevalence of obesity and associated morbidities described the use of anti-hypertensives and lipid lowering drugs, but did not consider other concomitant medications [26].

Given the knowledge gap, identification and consideration of the importance of obesity as a public health problem as well as the prioritization of medication safety in world agenda is important. This study aimed to analyze the prevalence of PDI and associated factors in severely obese patients.

2. Materials and Methods

2.1. Setting and Study Design

This study is a cross-sectional analysis of baseline data from the DieTBra Trial (Effect of Nutritional intervention and Olive Oil in Severe Obesity: Randomized Controlled Trial) with the following primary objective: to evaluate the effects of a nutritional treatment on inflammation, weight loss, and biochemical markers in severely obese individuals with a record in ClinicalTrials.gov, NCT02463435. In the trial protocol, all drug use variables and analyses were pre-specified in the baseline data. Patients were referred from the Brazilian Unified Health System (UHS) of primary healthcare to the nutrition and severe obesity outpatient clinic in a large university hospital in the Central-West region of Brazil. Excluded from the study were individuals that had already undergone bariatric surgery, were under actual nutritional treatment for weight loss or who in the previous two years used antiobesity drugs, had HIV/AIDS, had a heart/kidney/hepatic insufficiency, had a chronic obstructive pulmonary disease, cancer, or were pregnant. Further methodological details can be found in the DieTBra Trial articles with baseline data published elsewhere [27,28]. Data were collected from June 2015 to February 2016. All the participants gave their written consent to participate in this study, thereby conforming to the Helsinki declaration. This study was approved by Hospital of Clinics of Goiás Federal University research ethics committee with the registration number 1.545.504 in 08/14/2014.

2.2. Subjects

The subjects in the study included individuals aged 18 to 65 years with BMI ≥ 35 kg/m² referenced from primary care to the outpatient clinic specializing in the care of severely obese patients. Individuals residing outside the metropolitan area; who had already undergone bariatric surgery in the last three months which reduced more than 8% of their weight; who had received treatment in the same outpatient clinic; and those currently being treated for obesity, pregnant women, infants and those with special needs were excluded. Figure 1 shows the flow diagram of the enrolment of study patients.

2.3. Variables

The outcome variable was the presence of PDI. Firstly, the Micromedex[®] database was searched for all the drugs used by the patients to identify PDI. Then, a reclassification of PDI was made as present, when at least one PDI was identified, and absent, when no PDI was identified. The PDIs were classified into four categories according to the severity: namely, contraindicated, major, moderate, and minor according to the Micromedex[®] categories [29]. The contraindicated category included conditions

where drugs are contraindicated for concomitant use. The major category included conditions where the interaction may be life-threatening and/or require medical intervention to decrease or avoid serious adverse effects. The moderate category was defined as the condition in which the interaction may result in an exacerbation of the patient's health problem and/or require a change in treatment. The minor category included cases wherein the interaction would result in limited clinical effects, and where the manifestations may include an increased severity of side effects but do not demand a major change in treatment [29].

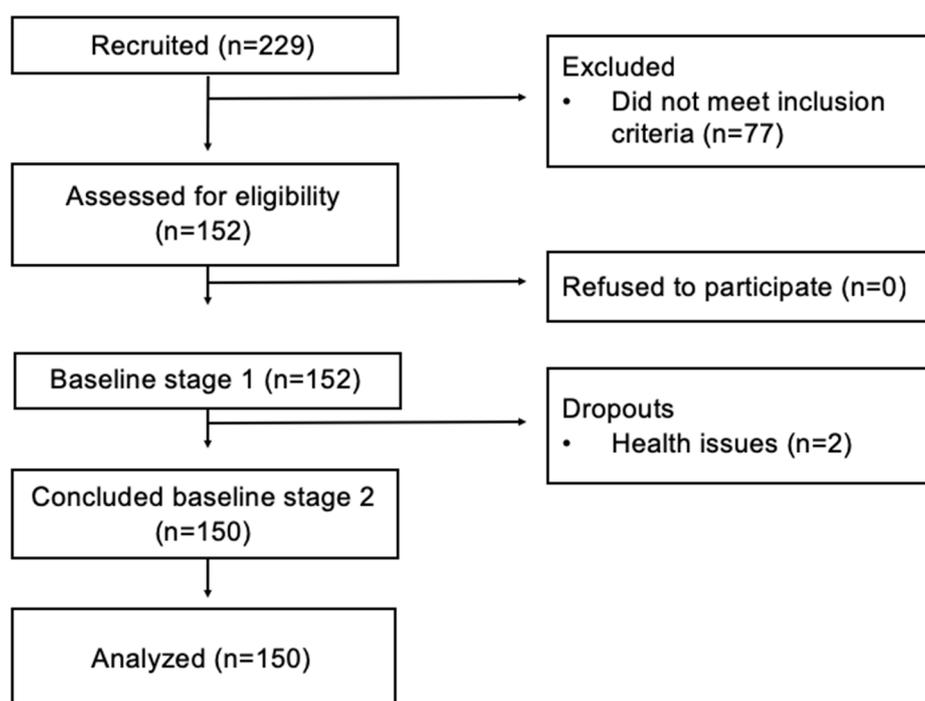


Figure 1. Flow diagram of the study patients' enrollment.

The explanatory variables were divided into four levels: socio-demographic, lifestyle, health, and drug use.

Socio-demographic: sex, age, years of study, skin color, living with partner, and economic class according to Brazil's standard economic classification criteria [30].

Lifestyle: the consumption of alcoholic beverages was estimated by questioning the patient about the amount of alcohol consumed the previous week [31]. Smoking was categorized under "non-smoker", "ex-smoker," and "smoker" [32].

Health: body mass index (BMI) was calculated by dividing the body weight into kg and height in meters squared. Patients with BMI ≥ 35 kg/m² and BMI ≥ 40 kg/m² were classified as having grade II obesity and grade III obesity, respectively [33]. AH was classified by blood pressure levels higher than 140/90 mm/Hg [34] and the use of antihypertensive drugs. DM was classified by fasting plasma glucose values ≥ 126 mg/dL [35] and the use of anti-diabetic drugs. Hypercholesterolemia was classified by the presence of one or more of the following conditions: isolated hypercholesterolemia, isolated hypertriglyceridemia, mixed hyperlipidaemia or low-density lipoprotein [36], and the use of anti-lipemic drugs. The number of self-reported morbidities [33] consisted of the number of diseases reported by the patient at the interview time.

Drug use: the use of drugs that cause weight gain [24,37–39] and polypharmacy, which is the practice of using five or more drugs [40], were categorized as “yes” and “no”. The practice of self-medication [41] was assessed using the question: “Do you have a prescription?” for each drug used by the patient and the answer was classified as “yes” or “no” according to the patient’s habit of using non-prescription drugs. The drugs used by the patient were classified according to the Anatomical Therapeutic and Chemical Classification (ATC) [42]. Associations of drugs not found on the ATC classification and phytotherapeutic drugs were categorized as non-classifiable (NC).

2.4. Data Collection

Patients enrolled in the study were interviewed by members of the research team who were appropriately trained to collect the socio-demographic data. Data regarding drug therapy were obtained by a pharmacist on the research team. Anthropometric data and health status were collected by a nutritionist on the research team. All members of the research team were trained according to standard operating procedures of the clinical trial.

2.5. Statistical Analyses

The association of variables was tested using the Pearson’s Chi-square test, Fisher’s exact test, or square Chi test for a linear trend, with a significance level of 5%. Variables with a *p*-value of 0.20 in the bivariate analysis were included in a Poisson regression model. The measure of association between the variables was the prevalence ratio (PR), with a confidence interval (CI) of 95%. STATA software, version 14 was used for the analyses. Data were processed with double input and any inconsistencies were corrected promptly.

3. Results

150 patients were analyzed and the PDI prevalence was 50% ($n = 75$) (95% CI 41–58). Each patient had on average 1.54 PDI (SD \pm 0.20, 95% CI 1.13–1.05). Approximately 84% ($n = 63$) of PDI were due to the use of non-prescription drugs. A total of 236 pairs of drugs with PDI were analyzed. Regarding the severity of potential drug interactions, most 98.72% ($n = 233$) were contraindicated, major and moderate. Among these, the most frequent pairs were ethinylestradiol + caffeine and diclofenac + losartan, with 93.0% ($n = 14$) and 5.08% ($n = 12$), respectively. The only contraindicated association observed was between trametamol ketorolac + naproxen (0.42%). Among the major cases, the association with diclofenac + hydrochlorothiazide was the most prevalent, with 10.53%. Among the associations considered as less severe, 10.22% ($n = 14$) occurred with ethinylestradiol + caffeine, and 8.76% ($n = 12$) with diclofenac + losartan (Table 1).

There was no association between PDI and socio-demographic variables and lifestyle (Table 2). A statistically significant association was observed between the health and medication use variables and the occurrence of PDI with hypertension, diabetes, number of self-reported morbidities, use of drugs that cause weight gain, and polypharmacy (Table 3). After the multiple analyses by Poisson regression, the variables that remained associated with the occurrence of PDI were hypertension (PR 1.83, 95% CI 1.10–3.04), polypharmacy (PR 3.12, 95% CI 2.17–4.50), and diabetes (PR 0.60, 95% CI 0.45–0.81) (Table 4).

The therapeutic classes most associated with occurrence of PDI were alimentary tract and metabolism ($p < 0.001$), blood and blood forming organs ($p = 0.005$), cardiovascular system ($p < 0.001$), systemic hormonal preparations, excluding sex hormones and insulin ($p = 0.001$), and musculoskeletal system ($p < 0.001$) (Table 5).

Table 1. Potential drug interactions more prevalent in adults with severe obesity according to severity and clinical management.

Severity	n	%	More Prevalent Pairs of Drugs with Potential Drug Interactions	Management *
Contra-indicated	1	0.42%	Trometamol cetrolac + Naproxen	Concurrent use may cause in enhanced gastrointestinal adverse effects (peptic ulcers, gastrointestinal bleeding and/or perforation).
Major	95	40.25%	Diclofenac + Hydrochlorothiazide	Concurrent use may result in impaired renal function. When co-administration is required, monitor renal function at the beginning and during treatment, as well as blood pressure control.
			Acetylsalicylic acid + Metformin	Concomitant use may cause hypoglycemia. A more frequent monitoring of blood glucose is suggested. Advise patients to recognize early signs and symptoms of hypoglycemia.
			Diclofenac + Acetylsalicylic acid	Concurrent use may result in impaired renal function. When co-administration is required, monitor renal function at the beginning and during treatment, as well as blood pressure control.
			Diclofenac + Fluoxetine	Concurrent use results in an increased risk of bleeding. Monitoring the patient for signs and symptoms of bleeding may be necessary.
Moderate	137	58.05%	Hydrochlorothiazide + Acetylsalicylic acid	Concurrent use may result in impaired renal function. When co-administration is required, monitor renal function at the beginning and during treatment, as well as blood pressure control.
			Ethinylestradiol + Caffeine	Concurrent use may cause central nervous stimulation and insomnia. Advise patients to decrease caffeine intake while using contraceptives.
			Diclofenac + Losartan	Concurrent use may result in impaired renal function. When co-administration is required, monitor renal function at the beginning and during treatment, as well as blood pressure control.
			Hydrochlorothiazide + Enalapril	Concurrent use may result in an excessive increase in blood pressure reduction. At the beginning of therapy, it may be necessary to decrease diuretic dose or increase salt intake. If such measures are not effective, reduce the initial dose of Enalapril.
			Hydrochlorothiazide + Propranolol	Concurrent use may cause changes in patient’s glycemic and lipid profile. Monitoring of such parameters is suggested.
			Enalapril + Metformin	Concomitant use may cause hypoglycemia. A more frequent monitoring of blood glucose is suggested. Advise patients to recognize early signs and symptoms of hypoglycemia.
			Captopril + Metformin	Concomitant use may cause hypoglycemia. A more frequent monitoring of blood glucose is suggested. Advise patients to recognize early signs and symptoms of hypoglycemia.
			Hydrochlorothiazide + Salbutamol	Concurrent use may increase the risk of hypokalemia as well as changes in electrocardiogram. Monitoring of potassium levels as well as cardiac function is recommended.
			Diclofenac + Captopril	Concurrent use may result in impaired renal function. When co-administration is required, monitor renal function at the beginning and during treatment, as well as blood pressure control.
			Hydrochlorothiazide + Captopril	Concurrent use may result in an excessive increase in blood pressure reduction. At the beginning of therapy, it may be necessary to decrease diuretic dose or increase salt intake. If such measures are not effective, reduce the initial dose of Captopril.
			Levothyroxine + Omeprazole	Concurrent use may compromise the efficacy of Levothyroxine. Advise patient to use Levothyroxine four hours before or after omeprazole. Monitoring of TSH levels is suggested.
Total	233 ¹	98.72 ²		

¹: One patient could have more than a pair of drug interactions. ²: The remaining 1.72% are related to potential drug interactions without clinical relevance. * Truven Health Analytics. Micromedex. 2017 [29].

Table 2. Prevalence of Potential Drug Interactions (PDI) and its association with sociodemographic and lifestyle variables in adults with severe obesity (*n* = 150).

Variables	<i>n</i> (%)	PDI Presence	PR (CI 95%)	<i>p</i> Value
Sex				
Female	128 (85.33)	63 (49.22)	1.00	0.644 *
Male	22 (14.67)	12 (54.55)	0.90 (0.59–1.37)	
Age				
18–39	76 (50.67)	34 (44.74)	1.00	0.139 **
40–49	53 (35.33)	28 (52.83)	1.18 (0.82–1.68)	
≥50	21 (14.00)	13 (61.90)	1.38 (0.90–2.10)	
Years of study				
<10 years	75 (50.00)	36 (48.00)	1.00	0.624 *
>10 years	75 (50.00)	39 (52.00)	1.08 (0.78–1.49)	
Skin color				
White	46 (30.67)	21 (45.65)	1.00	0.530 **
Brown	83 (55.33)	43 (51.81)	1.13 (0.77–1.65)	
Black	21 (14.00)	11 (52.38)	1.14 (0.68–1.92)	
Economic class				
Class A/B	34 (22.67)	18 (52.94)	1.13 (0.76–1.66)	0.556 *
Class C	92 (61.33)	43 (46.74)	1.00	
Class D/E	24 (16.00)	14 (58.33)	1.24 (0.83–1.86)	
Lives with partner				
Yes	55 (36.67)	28 (50.91)	1.02(0.73–1.43)	0.865 *
No	95 (63.33)	47 (49.47)	1.00	
Smoking				
Non-smoker	101 (67.33)	48 (47.52)	1.00	0.384 *
Smoker/Ex-smoker	49 (32.67)	27 (55.10)	1.15 (0.83–1.60)	
Alcohol intake ¹				
No	13 (15.48)	5 (38.46)	1.00	0.318 *
Yes	71 (84.52)	38 (53.52)	1.39 (0.67–2.87)	

* Pearson’s Chi-square, ** Linear trend Chi-square, ¹ *n* = 84.

Table 3. Prevalence of Potential Drug Interactions and its association with health profile and drug use variables in adults with severe obesity (*n* = 150).

Variables	<i>n</i> (%)	PDI Presence	PR (CI 95%)	<i>p</i> Value *
Body Mass Index				
35–39	27 (18.00)	13 (48.15)	1.00	0.832
≥40	123 (82.00)	62 (50.41)	1.04 (0.68–1.60)	
Arterial Hypertension				
No	65 (43.33)	15 (23.08)	1.00	<0.001
Yes	85 (56.67)	60 (70.59)	3.05 (1.91–4.87)	
Diabetes				
No	90 (60.00)	38 (42.22)	1.00	0.020
Yes	60 (40.00)	37 (61.67)	1.46 (1.06–2.00)	
Hypercholesterolemia				
No	94 (62.67)	45 (47.87)	1.00	0.500
Yes	56 (37.33)	30 (53.57)	1.11 (0.80–1.54)	
Self-reported morbidities				
≤3	89 (59.33)	30 (33.71)	1.00	<0.001
≥4	61 (40.67)	45 (73.77)	2.18 (1.57–3.03)	
Drugs that cause weight gain				
No	106 (70.67)	42 (39.62)	1.00	<0.001
Yes	44 (29.33)	33 (75.00)	1.89 (1.41–2.53)	
Self-medication				
0	23 (15.33)	12 (52.17)	1.13 (0.72–1.78)	0.463
1–2	89 (59.33)	41 (46.07)	1.00	
≥3	38 (25.33)	22 (57.89)	1.25 (0.88–1.78)	
Polypharmacy				
No	101 (67.33)	29 (28.71)	1.00	<0.001
Yes	49 (32.67)	46 (93.88)	3.26 (2.38–4.48)	

* Pearson’s Chi-square.

Table 4. Multivariate analysis by Poisson Regression.

Variables	Adjusted Prevalence Ratio	Adjusted CI 95%	p Value *
Arterial Hypertension			
No	1		
Yes	1.82	1.10–3.04	0.020
Diabetes			
No	1		
Yes	0.60	0.45–0.81	0.001
Drugs that cause weight gain			
No	1		
Yes	1.35	0.99–1.84	0.059
Polypharmacy			
No	1		
Yes	3.12	2.17–4.50	<0.001

* Poisson Regression.

Table 5. Prevalence of drugs involved in Potential Drug Interactions distributed by Anatomical Therapeutic and Chemical Classification (ATC) in adults with severe obesity (n = 150).

	ATC Classification	n (%)	PDI Presence	p Value
A	Alimentary Tract and metabolism	57 (38.00%)	39 (68.42%)	<0.001 *
B	Blood and forming blood organs	11 (7.33%)	10 (90.91%)	0.005 **
C	Cardiovascular system	65 (43.33%)	48 (73.85%)	<0.001 *
D	Dermatologicals	0	0	-
G	Genito urinary system and sex hormones	12 (8.00%)	7 (58.33%)	0.547 *
H	Systemic hormonal preparations, excluding sex hormones and insulins	10 (6.67%)	10 (100%)	0.001 **
J	Antiinfectives for systemic use	6 (4.00%)	4 (66.67%)	0.341 **
L	Antineoplastic and immunomodulating agents	0	0	-
M	Musculo-skeletal system	97 (64.67%)	60 (61.86%)	<0.001 *
N	Nervous system	86 (57.33%)	44 (51.16%)	0.741 *
P	Antiparasitic products, insecticides and repellents	1 (0.67%)	0 (0.00%)	-
R	Respiratory system	17 (11.33%)	10 (58.82%)	0.440 *
S	Sensory organs	1 (0.67%)	0 (0.00%)	-
V	Various	0	0	-
NC	Non-Classifiable	16 (10.67%)	10 (62.50%)	0.290 *

* Pearson’s Chi-square, ** Fischer Exact Test.

4. Discussion

According to the literature, this is the first study to evaluate the drug use profile in severely obese patients associated with the occurrence of PDI and other variables on health conditions. It is increasingly relevant to know the health aspects and risks in severe obesity, since obesity is the fastest growing health condition in the world [1], and the one of greatest risk of aggravations and consequent mortality. The presence of PDI was elevated among the severely obese in association with other morbidities such as diabetes and hypertension, in addition to polypharmacy. Obesity and the morbidities associated with obesity, such as hypertension and diabetes [6], demand the use of more drugs, leading the patient to polypharmacy, which further increases the likelihood of occurrence of PDI. Our study demonstrated that polypharmacy increased the risk of the severely obese patient presenting PDI more than three-fold.

Although previous studies related to the prevalence of PDI in severely obese individuals are not available, such outcomes have been described in studies on patients with chronic health conditions [22,23]. The prevalence of PDI in the present study was higher than observed in a study with the elderly (36.9%) [22], and less than in onco-haematological patients (71.3%) [23]. This variability in prevalence may occur due to differences between patient/morbidity, study sites, and countries [43].

These findings reinforce the need for further studies regarding drug use in the severely obese, to establish the patterns of use and therapeutic classes more associated with PDI and their clinical relevance.

In our study, the association with AH and PDI was observed. A clinical explanation for this result may be the difficulty of pharmacological control of AH monotherapy in obese individuals [5]. The achievement of satisfactory blood pressure levels is a problem in clinical practice in obese patients due to the increased activity of the renin-angiotensin system and aldosterone, which decreases the efficacy of pharmacological treatment [5]. The addition of multiple drugs may be necessary to achieve appropriate blood pressure levels in these patients [3], which leads to an increased risk of developing PDI.

As in AH, DM treatment is also commonly performed with drug associations [44], partially explaining the observed association between PDI and DM. Although the pathophysiology associated with refractoriness to pharmacological treatment of DM in the severely obese is still unknown, in some cases, it may be caused by impaired pharmacokinetics and the bioavailability of drugs because of changes in the volume of distribution [45], the liver [9], and renal function [46]. It is suggested that adequate glycemic control may not be achieved due to the exposure of sub-therapeutic doses, which leads to the addition of other drugs to the therapeutic regimen [44], which, consequently, increases the possibility of the occurrence of PDI.

Polypharmacy is a reality among patients with chronic conditions [47]. Although necessary, polypharmacy should be done with caution, since it is associated with the occurrence of PDI, as observed in the present study and described in previous studies [48]. It is known that PDI may be associated with the occurrence of adverse drug reactions [49], as well as increased hospitalization time [20]. Although no other research was found addressing polypharmacy and the prevalence of PDI in obese patients, this study's results are in line with other studies in patients with chronic diseases [21–23]. In obese patients, these complications may have more serious consequences, such as the onset of serious adverse reactions and a difficulty in controlling comorbidities.

Although sociodemographic variables have not demonstrated an association with the occurrence of PDI, these results are in line with those of other studies. Sex and age were not associated with the occurrence of PDI in a study conducted in onco-hematological patients [23] and the institutionalized elderly, as well as the marital status and schooling in the latter case [43]. The occurrence of PDI in obese individuals seems to be more associated with clinical aspects and morbidities than sociodemographic variables.

The drugs that act in the digestive system and metabolism were associated with the occurrence of PDI, which may be partially explained by the presence of antidiabetics. These drugs' metabolism is made by the enzymatic systems involved in the metabolism of other drugs, which may result either in therapeutic ineffectiveness or in a safety problem [50].

The occurrence of PDI associated with cardiovascular and musculoskeletal system drugs may be partly explained by the influence of non-steroidal anti-inflammatory drugs on the action of antihypertensives. The result of such PDI is already well described in the literature, and it decreases the effects of antihypertensives to control patients' blood pressure levels [51,52]. Since obese patients commonly suffer from back, knee, and ankle pain, among others [10], therapy with nonsteroidal anti-inflammatory drugs may be necessary [53]. This is a PDI of clinical importance due to its potential for patient harm. There is evidence suggesting the raise of serum creatinine in patients in the use of NSAIDs [52] and this is a parameter that must be monitored during concomitant therapy. The raise of serum creatinine may lead to renal failure and consequently may affect blood pressure control [51]. This is a relevant aspect, especially in the severely obese, because it increases the risk of cardiovascular events [36]. Healthcare professionals must be aware of the risk and its clinical management to identify the reduction of AH treatment effectiveness.

As a possible limitation of this research we could mention the number of patients and their conduction in a single center. However, we emphasize that the results are consistent and relevant to the field of obesity, especially of the severe obese, with a few studies. Although drug use variables and

their statistical analysis were not detailed in the clinical trial protocol, all details on this topic were part of a specific objective of original study and were pre-specified in the protocol approved by the local ethics committee. We highlight that all requirements for good clinical research practices were met and strict quality control criteria and methodological rigor were followed in all stages of the research. This study has great importance for clinical practice, as it is the first to analyze the occurrence of PDI and associated factors in severely obese patients. PDI are a major problem among individuals with severe obesity due to their high prevalence and association with other morbidities. However, PDI are susceptible to prevention and management if they are recognized and monitored, so knowing the factors associated with their occurrence has great importance for health professionals.

5. Conclusions

The presence of PDI in the present study was observed in 50% of patients and associated with DM, AH, and polypharmacy. Some drugs belonging to the first level of ATC classification have been shown to be associated with the onset of DIP: namely, alimentary tract and metabolism, blood and blood forming organs, cardiovascular system, systemic hormonal preparations, excluding sex hormones and insulins and the musculoskeletal system. Considering the PDI as a potential source of damage, especially in individuals with multimorbidities, such as the severely obese, a detailed review of the medications in use can prevent the manifestation of undesirable outcomes for the patient.

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