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Adverse Events Reported with the Use of Mazindol in Adult Obese Mexican Patients

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Abstract

Background: Obesity is a pandemic disease. Lifestyle modifications as diet and exercise remain as the first-line intervention for obesity; however, many patients fail to attain adequate weight loss and require drug treatment. Mazindol is a short-term useful agent in the treatment of obesity, whose safety profile has not been analyzed in Mexican population.

Objective: The current study was performed to investigate the reports of adverse events, received in the supplier laboratory for 8 years (2009-2016) with the purpose of determine potential issues of safety, related to Mazindol (MZ1®).

Methods: Adverse events were arranged in frequency tables and stratified by intensity and causality. Subgroups of sex, age and BMI with a higher frequency of side-effects were identified, as well as the main comorbidities and concomitant medications.

Results: One thousand three hundred eighty-six adverse events from 581 reports were received from 2009 to 2016. Most of reports were generated by patients in the fourth decade of life in both groups (25.5%). The most frequent adverse events were dry mouth (17.2%), polydipsia (10.6%) and constipation (9.0%). Most of them were both mild (90.5%) and possible (59.2%). Constipation was an important cause of withdrawal.

Conclusions: Data seems to indicate that 1 mg Mazindol is well tolerated for obesity treatment and its adverse events profile is acceptable. However, it is necessary to emphasize in the use appropriate of the drug, following the dosage schedule and indications approved.

Keywords: Adverse events; Mazindol; Mexican; Obesity; Pharmacotherapy; Safety

Introduction

Obesity is consequence of an excessively high accumulation of body fat or adipose tissue in relation to lean body mass, which could result harmful to health [1,2]. World Health Organization defines overweight as a body mass index (BMI) between 25-29.9 kg/m^2 and obesity as a BMI ≥ 30 kg/m^2 [2]. The prevalence of obesity is especially worrisome in Mexico and United States of America, where around 70% of adults are obese or overweight [3,4]. Obesity significantly raises the risk of chronic and disabling diseases such as hypertension, dyslipidemia, heart disease, diabetes, sleep apnea and osteoarthritis, among others [5-10]. On the contrary, it is known that a body weight reduction greater than 3% diminishes the cardio metabolic risks of obese patients [10,11].

Diet and exercise are the bases of anti-obesity therapy; unfortunately, this intervention shows low adherence and a poor success rate. Pharmacotherapy for obesity is indicated for individuals with BMI ≥ 30 kg/m^2 or those adults with BMI ≥ 27 kg/m^2 and comorbidities [10,12].

Mazindol is a stimulant drug of the tetracyclic chemical class developed in the 1960s, which constitutes a useful agent in the adjunctive short-term treatment of exogenous obesity in combination with dietary programs and exercise [13]. Although, its mechanism of action has not been completely elucidated, Mazindol seems to inhibit norepinephrine, serotonin and dopamine re-uptake to reduce appetite [14,15]. Several studies have documented the efficacy of Mazindol over placebo as an effective weight-reducing agent, which produces around 7 kg of weight loss, at twelve weeks [16-21]. In spite the several gastrointestinal, neurological, cardiovascular and endochrinological adverse events related with the use of Mazindol, it has been stated this product is especially useful in patients with mild-to-moderate hypertension, hyperlipidemia and diabetes mellitus, producing few adverse effects, and also in the treatment of patients with sleep disorders, as the incidence of central nervous stimulation is low with Mazindol [22-24].

In Mexico, the studies or reports on pharmacovigilance are scarce. The current study analyzed the spontaneous reports of adverse events, received in the supplier laboratory for 8 years (2009-2016) with the purpose of determine potential issues of safety, related to Mazindol (MZ1®) in Mexican users.

Methods

Adverse events associated to 1 mg Mazindol tablets (MZ1®) were obtained from a database generated by the supplier laboratory during 8

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years (2009-2016). In all cases, the prescribed dose corresponded to the fasting intake of one tablet a day before breakfast.

Adverse events were arranged by their seriousness as 1) mild: the adverse event was well tolerated and its resolution did not involve medication, hospitalization or ending the treatment; 2) moderate: the adverse event affected normal daily activity but without risking life and its resolution could require medication, but not necessarily ending the treatment; and 3) severe: the adverse event interfered normal daily activity, needed medication and ending the treatment.

Moreover, adverse events were stratified by causality as 1) certain: there was laboratory test abnormality and the adverse event occurred in a plausible time relationship to drug administration and it could not be attributed to a concurrent disease or other drugs or chemicals; 2) likely: there was laboratory test abnormality and the adverse event showed a reasonable time sequence to drug administration, it could not be associated to concurrent disease or other drugs or chemicals and, it followed a clinically reasonable response on dechallenge; 3) possible: there was laboratory test abnormality and the adverse event presented a reasonable time sequence to drug administration, but it could also be explained by concurrent disease or other drugs or chemicals and, the information on dechallenge was lacking or unclear; 4) unlikely: there was laboratory test abnormality, but the adverse event indicated an improbable causal relationship, which could be explained by other drugs, chemicals or underlying disease. 5) Unclassified: there was laboratory test abnormality, but more data was essential for a proper assessment; and 6) unclassifiable: the adverse event had insufficient or contradictory information, which could not be supplemented or verified [1].

Adverse events were also grouped by age, sex and BMI to determine the main subgroups affected by the drug treatment. Furthermore, most commonly concomitant drugs and concurrent diseases were established. Data are presented as frequency values in tables.

Results

Number of reports and demographic data

Table 1 exhibits the demographic data of 581 patients, who reported 1386 spontaneous adverse events with the use of 1 mg of Mazindol. Women reported the most of adverse events, corresponding to more than 89% of all reports. Likewise, physicians made 97.1% (1346) of adverse event reports, whereas patients only reported 2.9% (40) of side-effects. Age in men was a little bit lower than in women. Men also presented higher weight, height and BMI respect to women.

Adverse events associated with mazindol, by age, BMI and sex

Figure 1 shows data on the number of patients that presented adverse events using 1mg Mazindol, arranged by age and sex (Figure 1A) or BMI and sex (Figure 1B). Adverse events were detected, mainly in the fourth decade of life in both sexes. There were reports on 32 patients younger than 18 years (25 women and 7 men). This group presented mild adverse events, mainly dry mouth (14 patients), polydipsia (12 patients) and one case of hypertension, constipation, dizziness, nausea, emesis and hypotension. Two hundred eighty patients treated with 1 mg of Mazindol suffering adverse events had a BMI ≥ 30 kg/m^2; the rest of them had only overweight (259 patients) or normal weight (42 patients).

Global frequency, severity and causality of adverse events associated with mazindol

Table 2 shows the frequency of each adverse event reported for 1 mg Mazindol. By far, the main adverse events were gastrointestinal or neurological. Dry mouth, polydipsia and constipation were the most frequent adverse events reported with the use of 1 mg Mazindol, followed by headache, dizziness, insomnia, thirst, anxiety and nausea. Moreover, 37 reports were of lack of efficacy, 24 cases of weight gain, and 23 reports of mismanagement of the drug by increasing the prescribed dose by the own patient. There were few cardiovascular, dermatological, genitourinary or endocrinological reports. In addition, 1242 adverse events corresponded to women (approximately 90%) and 144 to men (approximately 10%), which followed a similar pattern regarding the most frequent individual adverse events.

Table 3 shows the data collected on the moderate or severe intensity of adverse events. Most of adverse events were mild (1255 adverse events); a few moderate (55 adverse events), where just one man suffered a moderate increased blood pressure. The main moderate adverse events were constipation (16 reports) and headache (8 reports).

Parameter	F	M
Sex†	516 (88.8)	65 (11.2)
Age (years)‡	41.6 ± 13.5	36.2 ± 13.0
Weight (kg)‡	73.5 ± 12.6	92.6 ± 14.5
Height (cm)‡	155.8 ± 6.4	169.4 ± 5.8
BMI (kg/m^2)‡	31.0 ± 5.6	33.8 ± 7.8

Data are presented as † the number of patients (%) or as ‡ mean ± standard deviation. Abbreviations: BMI=body mass index, F=female, M=male.

Table 1: Demographic data of patients reporting spontaneously adverse events with the use of 1 mg of Mazindol.

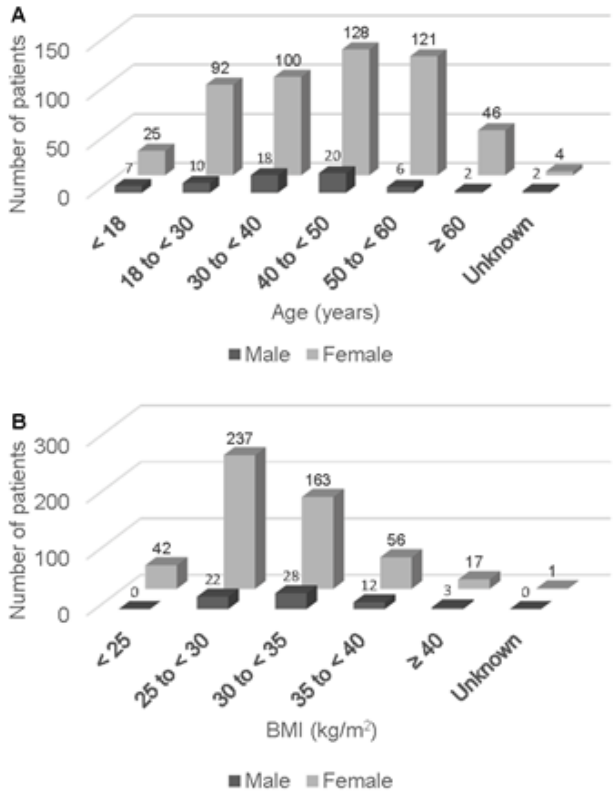

Figure 1: Number of patients showing adverse events associated with the use of 1 mg of Mazindol, which were stratified by age and sex (A) or age and BMI (B). Data are presented as the number of adverse events. Abbreviation: BMI=body mass index, F=female, M=male.

Adverse event	F	M	Adverse event	F	M	Adverse event	F	M
Dry mouth	208 (15.0)	30 (2.2)	Extremity pain	3 (0.2)	--	Crying	1 (0.1)	--
Polydipsia	130 (9.4)	17 (1.2)	Feeling cold	3 (0.2)	--	Delayed motility	1 (0.1)	--
Constipation	119 (8.6)	5 (0.4)	Hemorrhoid	3 (0.2)	--	Diaphoresis	1 (0.1)	--
Headache	76 (5.5)	5 (0.4)	Hypotension	3 (0.2)	--	Dysphagia	1 (0.1)	--
Insomnia	70 (5.1)	6 (0.4)	Increased hunger	3 (0.2)	--	Fine tremor	1 (0.1)	--
Dizziness	65 (4.7)	14 (1.0)	Myalgia	3 (0.2)	--	Gastritis	1 (0.1)	--
Thirst	65 (4.7)	2 (0.1)	Pruritus	3 (0.2)	--	Hyperthermia	1 (0.1)	--
Anxiety	54 (3.9)	2 (0.1)	Vertigo	3 (0.2)	--	Hypoacusia	1 (0.1)	--
Nausea	37 (2.7)	4 (0.3)	Blurred vision	2 (0.1)	2 (0.1)	Immunosuppression	1 (0.1)	--
Lack of efficacy	32 (2.3)	5 (0.4)	Depression	2 (0.1)	1 (0.1)	Impaired attention	1 (0.1)	--
Tachycardia	25 (1.8)	1 (0.1)	Urinary retention	2 (0.1)	1 (0.1)	Increased energy	1 (0.1)	--
Hyperphagia	22 (1.6)	1 (0.1)	Alopecia	2 (0.1)	--	Irritable bowel syndrome	1 (0.1)	--
Weight gain	21 (1.5)	3 (0.2)	Binge eating	2 (0.1)	--	Labile hypertension	1 (0.1)	--
Misuse	20 (1.4)	3 (0.2)	Chromaturia	2 (0.1)	--	Lethargy	1 (0.1)	--
Nervousness	20 (1.4)	3 (0.2)	Confusion	2 (0.1)	--	Maculopapular rash	1 (0.1)	--
Fatigue	18 (1.3)	1 (0.1)	Dry skin	2 (0.1)	--	Mastitis	1 (0.1)	--
Abdominal distention	14 (1.0)	--	Fear	2 (0.1)	--	Muscular weakness	1 (0.1)	--
Hyperhidrosis	12 (0.9)	3 (0.2)	Neck pain	2 (0.1)	--	Nycturia	1 (0.1)	--
Paresthesia	12 (0.9)	1 (0.1)	Pain	2 (0.1)	--	Restlessness	1 (0.1)	--
Drowsiness	10 (0.7)	2 (0.1)	Piloerection	2 (0.1)	--	Seborrhea	1 (0.1)	--
Dysgeusia	10 (0.7)	--	Pyrosis	2 (0.1)	--	Syncope	1 (0.1)	--
Abdominal pain	9 (0.6)	--	Rectal bleeding	2 (0.1)	--	Soft stools	1 (0.1)	--
Chills	9 (0.6)	--	Steatorrhea	2 (0.1)	--	Speech disorder	1 (0.1)	--
Asthenia	7 (0.5)	2 (0.1)	Suffocation	2 (0.1)	--	Tachycardia	1 (0.1)	--
Emesis	7 (0.5)	2 (0.1)	Tinnitus	2 (0.1)	--	Temperature disorder	1 (0.1)	--
Tremor	7 (0.5)	1 (0.1)	Dysuria	1 (0.1)	2 (0.1)	Urinary tract infection	1 (0.1)	--
Irritability	6 (0.4)	1 (0.1)	Hypoglycemia	2 (0.1)	1 (0.1)	Vulvovaginal dryness	1 (0.1)	--
Dry lips	6 (0.4)	--	Hypertension	1 (0.1)	2 (0.1)	Decreased libido	--	2 (0.1)
Early satiety	6 (0.4)	--	Depressed mood	1 (0.1)	1 (0.1)	Erectile dysfunction	--	2 (0.1)
Hungry	6 (0.4)	--	Food craving	1 (0.1)	1 (0.1)	Testicular pain	--	2 (0.1)
Change of mood	4 (0.3)	1 (0.1)	General discomfort	1 (0.1)	1 (0.1)	Urinary incontinence	--	2 (0.1)
Acne	4 (0.3)	--	Abnormal feeling	1 (0.1)	--	Abnormal urinalysis	--	1 (0.1)
Diarrhea	4 (0.3)	--	Aggressiveness	1 (0.1)	--	Asthenopia	--	1 (0.1)
Dyspnea	4 (0.3)	--	Anger	1 (0.1)	--	Flank pain	--	1 (0.1)
Flatulence	4 (0.3)	--	Aphasia	1 (0.1)	--	Hemorrhoidal bleeding	--	1 (0.1)
Hypersomnia	4 (0.3)	--	Arrhythmia	1 (0.1)	--	Hypoactivity	--	1 (0.1)
Rash	4 (0.3)	--	Balance disorder	1 (0.1)	--	Rectal tenesmus	--	1 (0.1)
Stress	4 (0.3)	--	Breast tenderness	1 (0.1)	--	Testicular Swelling	--	1 (0.1)
Back pain	3 (0.2)	1 (0.1)	Bowel hypermotility	1 (0.1)	--	Urgent urination	--	1 (0.1)
Chest pain	3 (0.2)	--	Confusion	1 (0.1)	--			

Data are presented as the number of adverse events (%). Abbreviations: F=female, M=male.

Table 2: Number of adverse events spontaneously reported with the use of 1 mg of Mazindol, which were stratified by sex.

Adverse event	Moderate		Severe	
	F	M	F	M
Constipation	16 (23.5)	--	5 (7.4)	--
Headache	8 (11.8)	--	--	--
Abdominal pain	3 (4.4)	--	1 (1.5)	--
Insomnia	3 (4.4)	--	--	--
Abdominal distension	2 (2.9)	--	1 (1.5)	--
Diarrhea	2 (2.9)	--	--	--
Emesis	2 (2.9)	--	--	--
Fatigue	2 (2.9)	--	--	--
Hypoglycemia	2 (2.9)	--	--	--
Anxiety	1 (1.5)	--	--	--
Aphasia	1 (1.5)	--	--	--
Breast tenderness	1 (1.5)	--	--	--
Dizziness	1 (1.5)	--	1 (1.5)	--
Gastritis	1 (1.5)	--	--	--

Hemorrhoid	1 (1.5)	--	--	--
Irritable bowel syndrome	1 (1.5)	--	--	--
Myalgia	1 (1.5)	--	--	--
Nausea	1 (1.5)	--	--	--
Nervousness	1 (1.5)	--	--	--
Paresthesia	1 (1.5)	--	--	--
Pruritus	1 (1.5)	--	--	--
Rectal bleeding	1 (1.5)	--	--	--
Tachycardia	1 (1.5)	--	--	--
Hypertension	--	1 (1.5)	--	--
Back pain	--	--	1 (1.5)	--
Blurred vision	--	--	1 (1.5)	--
Headache	--	--	1 (1.5)	--
Hypotension	--	--	1 (1.5)	--
Syncope	--	--	1 (1.5)	--
Data are presented as the number of adverse events (%). Abbreviations: F=female, M=male.				

Table 3: Number of moderate and severe adverse events reported spontaneously with the use of 1 mg of Mazindol.

In addition, there were 13 severe adverse events in women, primarily constipation (5 reports). From severe adverse events, only the case of syncope was considered as serious.

With respect to its causation, 3 events were classified as certain (1 chromaturia, 1 irritability and 1 tachycardia), 7 events were likely (2 cases of binging, 1 seborrhea, 1 weight gain, 1 anxiety, 1 breast tenderness and 1 maculopapular rash), 495 reports were classified as probable and 821 reports were considered as unlikely. In addition, 60 reports were considered as unclassified (37 reports of lack of efficacy and 23 reports of intentional misuse).

Drug withdrawal

From total cases (581), in 158 of them was reported a single adverse event, 220 indicated 2 adverse events, in 98 there were 3 adverse events, in 58 cases were reported 4 adverse events, in 33 cases there were 5 adverse events, in 8 cases there were 6 adverse events, in 5 cases were reported 7 adverse events and in 1 case there were 8 adverse events. In 72.8% cases were reported two or more adverse events per patient (data no shown). Although, 90.5% of adverse events were mild, there were 115 cases of Mazindol withdrawal. In patients who suffered one adverse event occurred 67 drug withdrawals; mainly due to constipation, thirst, dry mouth, insomnia, lack of efficacy and weight gain. Moreover, there were only 3 withdrawals in men (Table 4).

Regarding the frequency of withdrawals caused by one or more relevant adverse events, constipation alone or combined with other adverse events produced 41 withdrawals. Dry mouth and lack of efficacy alone or plus other adverse event produced 21 withdrawals. Cardiovascular, dermatological or urinary adverse events alone or combined, also gave rise to an important number of withdrawals. Hypoglycemia produced 1 case of withdrawal, in combination with other six adverse events. It was remarkable the high frequency of genitourinary tract adverse events in men.

Concomitant medications or diseases

Tables 5 and 6 show the data on concomitant medicaments (141 patients) and diseases (361 patients). The most frequently co-used drugs were anti diabetic agents as metformin and glyburide, antihypertensive as Enalapril and Losartan, and a group of supplements, including Melatonin, Calcium, Vitamins and Minerals. Also, the use of thyroid hormones was registered in 9 cases.

Regarding comorbidities, diabetes mellitus (54 cases), hypertension (45 cases), venous insufficiency (45 cases), dyslipidemia (39 cases), constipation (31 cases) and insomnia (28 cases) were the most frequent.

Withdrawal	F	M	Withdrawal	F	M	Withdrawal	F	M
Constipation	17 (25.4)	--	Weight gain	6 (9.0)	--	Rash	1 (1.5)	--
Thirst	10 (14.9)	--	Lack of efficacy	6 (9.0)	--	Erectile dysfunction	--	1 (1.5)
Dry mouth	9 (13.4)	1 (1.5)	Dizziness	4 (6.0)	--	Hypertension	--	1 (1.5)
Insomnia	7 (10.4)	--	Headache	4 (6.0)	--			
Data are presented as the number of withdrawals (%). Abbreviations: F=female, M=male.								

Table 4: Number of withdrawals observed in patients with a single adverse event reported spontaneously with the use of 1 mg of Mazindol.

Medicament	F	M
Anti-diabetic drugs	29 (20.6)	8 (6.7)
Antihypertensive	29 (20.6)	4 (2.8)
Vitamins, minerals, lactobacilli and herbal supplements	21 (14.9)	--
Gastrointestinal drugs	15 (10.6)	--
Anti-varicose	7 (5.0)	--
Thyroid drugs	6 (4.3)	3 (2.1)
Non-steroidal anti-inflammatory drugs	6 (4.3)	1 (0.7)
Lipid-lowering drugs	4 (2.8)	2 (1.4)
Others	5 (3.5)	1 (0.7)
Data are presented as the number of patients with concomitant medications (%). Abbreviations: F=female, M=male.		

Table 5: Concomitant medications in patients who reported adverse events with the use of 1 mg of Mazindol.

Discussion

In this analysis on spontaneous adverse events related to 1 mg Mazindol, a higher number of women than men reported adverse events, which seems imply Mexican woman are the main users of anti-obesity drugs, rather than women are more susceptible to the adverse events of Mazindol. This sex difference on the anti-obesity drug users coincides with other reports [25-27], where female consume more anti-obesity drugs than male because the slimness culture as a symbol of beauty, which is more rooted on women [26,27].

In Mexico, Mazindol is a product of mandatory prescription, indicated as an adjunct in the treatment of exogenous obesity for adult individuals with BMI ≥ 30 kg/m^2 or BMI ≥ 27-29.9 kg/m^2 and

Disease	F	M	Disease	F	M	Disease	F	M
Diabetes mellitus	45 (12.5)	9 (2.5)	Irritable bowel syndrome	9 (2.5)	1 (0.3)	Bursitis	1 (0.3)	--
Hypertension	45 (12.5)	--	Cholelithiasis	5 (1.4)	2	Goiter	1 (0.3)	--
Venous insufficiency	40 (11.1)	5 (1.4)	Metabolic syndrome	5 (1.4)	1 (0.3)	Hemorrhoids	1 (0.3)	--
Dyslipidemia	33 (9.1)	6 (1.7)	Urinary incontinence	5 (1.4)	1 (0.3)	Hypertriglyceridemia	1 (0.3)	--
Constipation	30 (8.3)	1 (0.3)	Colitis	3 (0.8)	--	Lumbago	1 (0.3)	--
Insomnia	24 (6.6)	4 (1.1)	Asthma	2 (0.6)	--	Osteopenia	1 (0.3)	--
Gastritis	22 (6.1)	2 (0.6)	Hypercholesterolemia	2 (0.6)	--	Polycystic ovary	1 (0.3)	--
Gastro esophageal reflux	15 (4.2)	3 (0.8)	Osteoporosis	2 (0.6)	--	Slipped disc	1 (0.3)	--
Hypothyroidism	11 (3.0)	3 (0.8)	Acne	1 (0.3)	--	Allergic rhinitis	--	1 (0.3)
Fatty liver	10 (2.8)	3 (0.8)	Arthritis	1 (0.3)	--	Inguinal hernia	--	1 (0.3)
Data are presented as the number of patients with comorbidities (%). Abbreviations: F=female, M=male.								

Table 6: Comorbidities reported in patients who presented adverse events with the use of 1 mg of Mazindol.

concomitant obesity-related risk factors or diseases. In this analysis, there were several cases of adverse events of Mazinol 1 mg coming from users with normal BMI ≤ 25 kg/m^2, other under 18-years-old or a large number of cases with only overweight. Abuse of appetite-suppressant drugs has been mainly associated to amphetamines as benzphentamine, diethylpropion and phentemine due to their possible addiction potential [28,29]. However, a dramatic increase in the intentional misuse of weight loss drugs has been observed between adolescents in the last decade, especially in those with unhealthy weight loss practices, such as vomiting and fasting [30]. In the current analysis, not relevant cases of special toxicity were observed in 1 mg Mazindol users under 18 and those with BMI ≤ 25 kg/m^2, besides the fact that only 23 subjects with BMI between 27 to 30 kg/m^2 reported comorbidities such as diabetes mellitus, hypertension or dyslipidemia. In fact, in our study, the use of Mazindol in patients under 18 years produced only mild adverse events, which is in line with the report that Mazindol may be beneficial in adolescents, even in doses of 2 mg daily [31]. Notwithstanding, the frequent off-label use and the misuse with probable aesthetic purposes of anorectic products, considered by other authors [32,33] may be especially damaging since individuals may show common adverse events of stimulants abuse, as anxiety, paranoia and cardiac anomalies [31]. In this regard, it is important to emphasize in the implementation of interventions designed to reduce the misuse of prescription stimulants, regardless of whether the drug has a high tolerability in the short-term treatment for obesity, as Mazindol.

Adverse events most frequently reported by Mexican patients were of gastrointestinal (dry mouth, polydipsia, constipation, thirst and nausea) or neurological (headache, dizziness, insomnia, anxiety and fatigue) origin, and relatively few cases of cardiovascular, dermatological, endocrinological or genitourinary systems. In line with our results, a meta-analysis study shows that only insomnia and constipation were associated with the consumption of Mazindol [34]. A further analysis revealed us that in patients with comorbidities, only in 9 cases of minor adverse reactions, the basic problem worsened, whereas in patients with hypertension there were not reported increments in blood pressure and, only a subject of three, who had hypoglycemia was associated with concomitant administration of hypoglycemic agents. This profile of adverse events in Mexican patients is in line with the reported general set of adverse events and also with the statement that Mazindol is especially useful in patients with mild to moderate hypertension and diabetes mellitus [22,23]. Lucchetta et al. in their meta-analysis study shows that Mazindol was not associated to major adverse reactions [34]. In fact, it has been used Mazindol in the treatment of narcolepsy and attention-deficit/hyperactivity disorder, as the incidence of central nervous stimulation is relatively low with the use of Mazindol [24,35].

Interestingly, there were 67 cases of drug withdrawal related with just one mild adverse event, being constipation the main adverse event. Our data suggests that irrespective of the severity of the adverse event reported, the discomfort produced by an adverse event can be as important to remove the drug. Additionally, constipation associated with one or more adverse events was responsible for 41 additional withdrawals cases. It is evident that constipation is an adverse event that affects adherence to Mazindol. In addition to this, the prevalence of functional constipation in Mexico corresponds to 14.4%, with a female/male ratio 3:1 [36]. Thus, Mazindol co-administered with orlistat, could be a useful alternative in a select group of obese patients, providing potential anti-obesity synergy and, complementarity of pharmacological profiles to reduce the impact of constipation. Significantly, genitourinary disorders, associated with one or more adverse events, basically in men, generated withdrawal in 9 of 9 patients, highlighting that, although the frequency of genitourinary adverse events is low, it caused withdrawal of the drug, in all patients.

Thirty-seven cases of lack of efficacy, plus 24 other probable related cases of weight gain, 23 of hyperphagia and 6 of hunger, were reported as adverse event. However, it should be considered that these data correspond exclusively to the lowest dosage of Mazindol (1 mg/day), since in the schedule accepted for the use of this drug, the dose may increment to 1 mg every 8 hours with meals, and this scheme was not used. In addition, drug ineffectiveness and dry mouth were accompanying with one or more adverse events in 15 cases. It is fair to say that drug ineffectiveness and dry mouth in these 15 cases contrasts with the report that xerostomia is a marker of Mazindol anti-obesity efficacy [37].

Although the number of adverse events associated to 1 mg Mazindol during 8 years is restricted and there was no follow-up of them, our analysis seems show that 1 mg Mazindol has a favorable safety profile in the short-term treatment for obesity. However, it is important to emphasize in the use appropriate of the drug, following the dosage schedule and indications approved.

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Conflict of Interest

We have no conflict of interest to declare.

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