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Review Article

Review of the Roles of Health Professionals about the Use of Anorectics: A Narrative Review Article

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Abstract

Anorectic drugs have been misused and abused because the desire for weight loss has increased worldwide. To prevent the misuse and abuse of anorectic drugs, the roles of health professionals are important. Therefore, this narrative review about anorectic drugs was performed. The aim of this narrative review was to investigate types of anorectic drugs, drugs prone to misuse and abuse and the roles of health professionals-pharmacists, doctors and nurses. The studies on anorectics used globally were found via researches on scholarly databases related with health professionals in the field of public health. Here investigated anorectic drugs used worldwide and several supplements. In particular, this narrative review focused on drugs likely to be misused and abused (e.g., fenfluramine, orlistat, phendimetrazine, phentermine and sibutramine). In addition, the abuse and the side effects of anorectic drugs were investigated. To prevent the misuse and abuse of anorectic drugs, health professionals should prescribe, dispense and administer drugs carefully and provide educational programs. This narrative review considers the individual roles of and cooperation between health professionals and suggests the provision of appropriate policies and programs against the abuse of anorectics.

Key words: Roles of health professionals, anorectic drugs, anorectics, obesity, abuse, pharmacology, pharmacists, side effects of anorectics, cooperation between health professionals

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INTRODUCTION

Recently, the desire for weight loss, in particular in women has increased around the world. There are some ways to lose weights, such as eating habit modification, exercise, anorectics and bariatric surgery[1]. Among them, anorectic drugs were originally designed to cure people suffering from obesity or complications of obesity. However, some studies have reported the problems with the abuse of anorectics[2-18].

In this narrative review, it investigated anorectic drugs used worldwide (amfepramone, amphetamine, benzphetamine, diethylpropion, fenproporex hydrochloride, liraglutide, lorcaserin, naltrexone/bupropion, orlistat, phendimetrazine, phentermine, rimonabant, sibutramine and topiramnate)[1-7,19-23] and several supplements (α-amylase inhibitor, α-lipoic acid, caffeine, chitin, cocoa, dietary fiber, green tea, *Phyillyrea latifolia* leaves and rimonabant)[2,21,24-26].

Although anorectic drugs, such as, orlistat should only be used by overweight adults, Alli (OTC name of orlistat) can be purchased online regardless age or weight in the USA[26]. Accordingly, it focused on drugs likely to be misused or abused (e.g., fenfluramine, orlistat, phendimetrazine, phentermine and sibutramine) and investigated their abuse and side effects. To prevent the misuse and abuse of anorectic drugs, the roles of health professionals are indispensable. Pharmacists deliver interventions for weight management, help select and monitor anorectics and provide patients with comprehensive dietary advice and information[19,26-34]. Doctors assess patient's habits and provide counseling regarding weight loss[1,35-39] and nurses provide weight-related interventions and conduct training and organizational support for obesity management[40-42].

The objectives of this narrative review were to identify types of anorectic drugs (anorectics) likely to be misused or abused, to define the roles of health professionals, to determine levels of cooperation between health professionals and to suggest appropriate policies and programs. This narrative review will be able to stimulate health professionals, who have continued to make efforts to protect people from abuse of anorectics and will give an opportunity for health professionals to be more interested in the abuse of anorectics than now.

APPROACH TO A NARRATIVE REVIEW

It was conducted comprehensive study to obtain information on types of anorectics, their abuse and roles of health professionals in the context of anorectic abuse. Searches of PubMed, Science Direct and Google Scholar were conducted to identify documents published between 1996 and 2016. To identify overall information about anorectics including types and abuse aspects, it searched the following keywords: "Anorectics", ''Anorectic drug abuse", "Weight control drug", "Weight loss" and "Drug abuse". After collecting information about anorectics, it focused on the roles of health professionals in the prevention of anorectic abuse and then, it searched for the following keywords: "Anorectic abuse", "Health professional", ''Pharmacist'', "Doctor", "Nurse" and "Intervention". In particular, a search for ''Obesity" plus "Pharmacist" identified 153 papers, including 75 papers published during the last 5 years. Among 153 papers, it excluded duplicates from difference sites and checked the relevance with our narrative review. The criteria for choosing references was the roles of pharmacists, doctors, nurses and other health professionals about the abuse of anorectics and then 92 papers were excluded in the final reference list and it referred to four studies to figure out characteristics about narrative reviews[43-46]. Finally, it selected a total of 65 papers as references.

TYPES OF ANORECTICS

Anorectic drugs are being used worldwide (Table 1). Amfepramone is a schedule 3 controlled drug in the UK[47] and has been used to treat obesity for more than 50 years, but is abused due to its low-cost in Brazil[48]. In fact, about 1,277 adults who were using amfepramone in Southern Brazil, 81% had an anorectic prescription. Mean period of usage was 8.7 months[49].

Benzphetamine and diethylpropion are used for short term treatment and approved by FDA as schedule III and IV drug, respectively. They are used much less than phentermine, though they tend to suppress the appetite of patients. Also, they are possible to cause side effects and have considerable problems from latent ability about abuse[1].

In 1999, fenproporex was withdrawn from market in France because it is inefficient for treating obesity. At time of discontinuation, users experienced withdrawal syndromes including anxiety and nightmares followed by depression Pelissier-Alicot *et al.*[50].

Some anorectics, including phentermine are recommended for short term use. The US Food and Drug Administration (FDA) had approved 5 anorectic drugs, that were orlistat, lorcaserin, phentermine/topiramate, naltrexone/bupropion and liraglutide for long term use[1,19]. Although some weight loss drugs have been withdrawn because of severe side effects, the FDA and the European Medicines Agency (EMA) differ in terms of approvals and/or withdrawals of anorectics. Sibutramine, orlistat and

Table 1: Several kinds of anorectic drugs and supplements

Anorectics	Whether it is a composition of the medicine	Country	Study
Amfepramone	Medicine	UK, Brazil, France	De Carvalho e Martins *et al.*[22], UK Legislation[47], Da Silva *et al.*[48], De Lima *et al.*[49] and Pelissier-Alicot *et al.*[50]
Amphetamine	Medicine	Brazil	De Carvalho e Martins *et al.*[22]
Benzphetamine	Medicine	US	Patel[1]
Diethylpropion	Medicine	US	Patel[1]
Fenproporex hydrochloride	Medicine	Brazil	De Carvalho e Martins *et al.*[22]
Liraglutide	Medicine	USA, EU	Patel[1], Khorassani *et al.*[19], Chen[20] and Bray *et al.*[21]
Lorcaserin	Medicine	USA	Patel[1], Khorassani *et al.*[19], Chen[20], Bray *et al.*[21] and Krentz *et al.*[23]
Naltrexone/bupropion	Medicine	USA, EU	Patel[1], Khorassani *et al.*[19], Chen[20] and Bray *et al.*[21]
Orlistat[1-5]	Medicine	Sweden, USA, EU	Patel[1], Kallen[2], Khorassani *et al.*[19], Chen[20] and Bray *et al.*[21]
Phendimetrazine	Medicine	USA	Bolin *et al.*[5]
Phentermine	Medicine	USA	Patel[1], Hendricks *et al.*[3], Khorassani *et al.*[19], Chen[20], Bray *et al.*[21] and Krentz *et al.*[23]
Rimonabant	Medicine	Sweden	Kallen[2]
Sibutramine	Medicine	Sweden, Brazil	De Carvalho e Martins *et al.*[22]
Sympathomimetic amines	Medicine	Brazil	De Carvalho e Martins *et al.*[22]
Topiramate	Medicine	USA	Patel[1], Khorassani *et al.*[19], Chen[20] and Bray *et al.*[21]
α-amylase inhibitor	Supplement	China	Chen[20]
α-lipoic acid	Supplement	Bosnia and Herzegovina	Okanovic *et al.*[25]
Caffeine	Supplement	China	Chen[20]
Chitin	Supplement	China	Chen[20]
Cocoa	Supplement	China	Chen[20]
Dietary fiber	Supplement	China	Chen[20]
Green tea	Supplement	China	Chen[20]
Phillyrea latifolia leaves	Supplement	Turkey	Yazici-Tutunis *et al.*[24]

rimonabant have been used as anorectics for 15 years in Sweden and although sibutramine was withdrawn from the European market, it can be purchased on the web and is considered as a main drug for weight loss[2]. In Brazil, the drugs most used for weight loss are amphetamine, sympathomimetic amines (40.5%), amfepramone, fenproporex hydrochloride and sibutramine[23].

Rimonabant has been used for treatment of anti-obesity in Sweden. Rimonabant was reported that it had potential for malformation and health problems, such as pes equinovarus and coarctation of aorta in case study for infants from mothers who took rimonabant in early pregnancy[2].

Some agents, not medicines are also available for weight loss. For example, α-lipoic acid induced weight loss in over-weight diabetes mellitus type 2 patients[25] and *Phillyrea latifolia* leaves are considered weight loss agents due to their ability to reduce obesity associated with cellular problems[24].

Caffeine, cocoa and green tea have also been used to induce weight loss. Dietary fiber not digested carbohydrates can reduce weight by disturbing energy intake[21]. To lose weight, youths have abused OTC drugs and supplements including laxatives in the USA. However, these agents are not used to lose weight and abuse can cause severe health problems[26]. Though there is no evidence about losing weight, α-amylase inhibitor and chitin are used to decrease calorie intake by inhibiting nutrients, such as carbohydrates and fat, from absorption in the body[21].

ABUSE OF ANORECTICS

Young women in particular misuse and abuse drugs to reduce weight despite having a normal body weight after purchasing drugs illegally online. For this reason, it focused on anorectics likely to be misused or abused (e.g., fenfluramine, orlistat, phendimetrazine, phentermine and sibutramine) and investigated their abuse and side effects (Table 2).

In one Brazilian study, 31.1% of college students took anorectics prescribed by doctors (31.1%) and 17.8% took non-prescribed drugs[23]. After long-term treatment, abrupt cessation of fenfluramine and its derivative (dexfenfluramine) can induce depressive withdrawal symptoms[6,21]. The seriousness of the side effects of fenfluramine and its derivatives have been well discussed and include a significant risk of heart disease. For this reason, they were withdrawn from market in 1997[6-9].

In the case of orlistat, western countries, including the USA have mostly reported results of orlistat abuse, which is viewed as a compensatory behavior in those with an eating disorder. In India, orlistat is an abused OTC drug due to its availability, peer pressure and the desire to wear western dress[10]. Orlistat has also been misused among normal weight patients with bulimia nervosa and caused severe problems. Patients who took Alli (OTC name of orlistat) at ten times recommended doses, which surpasses the intensity of

Table 2: Abuse and side effects of anorectic drugs

Anorectic drugs	Features	Side effects	Study
Fenfluramine	Widely spread prescription in combination with phentermine	Withdrawal depressive symptoms	Vivero *et al.*[6]
		Cardiovascular risk	Cheung *et al.*[7]
	Increase of serotonin release	Damage to heart valves	Cambon and Leclercq[8]
			Comerma-Steffensen *et al.*[9]
Orlistat	Intestinal lipase inhibitor absorption	Gastrointestinal related problems	Cheung *et al.*[7], Deb *et al.*[10],
	Purging effects	steatorrhea, fecal incontinence, frequent or urgent bowel movements, flatulence with discharge, full-blown bulimia nervosa, fecal urgency, increased defecation	O'Connor[11], Cumella *et al.*[12] and Fernandez-Aranda *et al.*[13]
	Ease of availability in India and western countries like USA	Risk for fluid and electrolyte imbalances	
		Vulnerable to a sudden cardiac event	
		Sudden death	
		Reduction in the absorption of the fat soluble vitamins	
Phendimetrazine	An agonist as complementary therapy in cocaine dependence	Death(blood concentration was 300 ng mL^{-1})	Bolin *et al.*[5] and Hood *et al.*[14]
Phentermine	Efficient drug both for short-term and long-term weight management	Hypertension	Hendricks *et al.*[3]
		Vasoconstriction	Khorassani *et al.*[19]
		Vasculopathy	Cheung *et al.*[7] Skopp and Jantos[15]
	Only use for a few weeks	Mental illness	
Sibutramine	Obstruction against serotonin and noradrenalin reuptake (hypothalamus)	Transient thyrotoxicosis	Cheung *et al.*[7]
		Irregular uptake of radioisotope, thyroid-stimulating	Comerma-Steffensen *et al.*[9]
	Reliable agent for obesity	hormone receptor antibody and thyroperoxidase antibody were negative	Luque and Rey[16]
		Sympathetic nervous system	Kim *et al.*[17]
		Blood pressure and heart rate elevations	Florentin *et al.*[18]
		Major adverse cardiovascular events	

prescription orlistat, experienced more serious side effects. Also, patients that misused orlistat with laxatives experienced fluid and electrolyte imbalances, which sometimes resulted in a heart accident of medical concern or death[12]. Main side effects of orlistat are associated with the gastrointestinal tract and include fatty/oily stools, fecal incontinence, repeated or sudden bowel movements and flatulence[7,11,12].

Phendimetrazine is a prodrug for the monoamine releaser phenmetrazine and an anorectic that has an analogous process with norepinephrine[14,21]. Phendimetrazine is known as a treatment for patients with cocaine use disorder and has been reported to be associated with abuse in cocaine-dependent patients[5]. It was mentioned that sympathomimetric drugs, including phendimetrazine have potential for adverse effects similar to amphetamine, such as insomnia. Therefore, phemdimetrazine was used for short-term treatment (less than 12 weeks)[21].

Although some researchers have reported that phentermine does not induce dependence or withdrawal syndrome after short or long-term treatment[3,4] and through several studies, it is recommended that phentermine be taken for less than 12 weeks due to the possibility of addiction and uncertain long-term safety[7,15]. However, phentermine is often prescribed as off label and sold in the market as obermine, phenterex, obephe and etc., in US.[1] Phentermine has been associated with serious health problems, such as, hypertension, vasculopathy and mental illness[15].

Sibutramine is an anorectic and a serotonin and noradrenalin re-uptake inhibitor in the hypothalamus[17,18]. One Korean patient who ingested 280 mg of sibutramine presented thyrotoxicosis with thyroiditis[17]. In addition, sibutramine has been associated with elevations in blood pressure, heart rate and adverse heart events[7,18]. Also, it was reported that babies from mother who used sibutramine for anti-obesity tend to have high potential for serious malformation[2]. In 2010, sibutramine was withdrawn by the FDA and in European market due to the risk of cardiovascular events[7,9]. However, sibutramine is still sold through the internet and used for making some items which are not medical drugs but products related to anti-obesity[2].

Roles of pharmacists, doctors and nurses and the prevention of the abuse of anorectic drugs: To prevent the misuse and abuse of anorectic drugs, the roles of the health professionals are indispensable. Health professionals should pay attention to anorectic drugs because these drugs have often been abused by patients with an Eating Disorder (ED)[10]. In one case, a person with an ED misused Alli and experienced diarrhea. To prevent this type of accident, health professionals should monitor orlistat because it can be accessed easily and is prone to abuse in the short and long-term[51]. Attitudes of health professionals are also important because they effect obese patients[52].

Although guidelines have been established to support health professionals regarding the treatment of obesity in USA, UK and Europe[22] several barriers remain with respect to the counseling of obese patients. The main barriers are lack of time (76.8%), lack of patient interest (55.8%) and lack of reward/return (49.3%)[53]. Actually, many patients are not prepared to pay pharmacists for management of obesity[54].

Health professionals make efforts to ensure the appropriate use of anorectics. The roles of individual health professionals are shown in Table 3.

Roles of pharmacists: In Australia, pharmacists educate consumers about prevalently used anorectics[28]. As consumers regarded pharmacists as important health professionals for weight management, pharmacists are able to deliver appropriate advice about weight management. They can provide female consumers who need to manage weight with proper advice and knowledge about meal replacement products and herbal products[27]. In USA, to meet the need to manage weight effectively[32], pharmacists help consumers to choose and monitor anorectics properly[19] and reclassify anorectics by developing regulations regarding 3rd class of BTC (behind-the-counter) drugs[26]. In addition, they provide interventions for preventive health services in rural areas on a clinic basis with follow-up to manage weight loss extensively[30]. In USA, it would be better for pharmacists to combine both behavioral and pharmacological treatment. Also, there was a need to determine how to combine treatments properly, because many efficient, secure anorectic drugs were available on prescription and as OTC drugs[31]. In UK, many services for public health are provided including telephone counseling, which is efficient and cost-effective for long-term weight management[29]. Individuals can use a telephone or request person-to-person care, which is a more efficient approach for maintaining weight loss than education alone[30]. In Thailand and Kuwait, obese patients are provided with programs to improve behavior and knowledge about weight and obesity[33,34]. In Thailand, Primary Care Units (PCUs) provided pharmacists with the opportunity of establishing weight loss programs. Also, PCUs enable various health professionals, such as, doctors, nurses and community staff, to offer health services to satisfy needs related to local health[33]. In Kuwait, plans were proposed to create behavioral changes to increase physical performance and improve aspects related to eating. Some of these proposals included improving of information regarding obesity, counseling skills and raising patient awareness of the value of communicating with pharmacists[34].

Table 3: Roles of pharmacists, doctors and nurses against the abuse of anorectics

Group	Country	Roles	Study
Pharmacists	Australia	Provision of dietary advice for successful weight management	Fakih *et al.*[27]
		Education for consumers about prevalence of anorectics	
		Provision of information on meal replacement products and herbal products	
	USA	Extensive care by telephone or face-to-face	Perri *et al.*[30]
		Delivery of extended-care programs including clinic-based follow-up sessions	
		Delivery of interventions to rural areas through infrastructures for preventive health services	
		Assistance with ensuring selection and monitoring in drug using	Khorassani *et al.*[19]
		Needs for considerations relevant to altering the drug classification system	Pomeranz *et al.*[26]
	UK	Provision of public health service including telephone counseling	Brown *et al.*[29]
	Thailand	Delivery of weight management programs	Phimarn *et al.*[33]
		Collaboration of various health professionals, such as doctors, nurses and community staffs for health services	
	Kuwait	Improvement of eating behavior and knowledge about weight and obesity, personal physical level and aspects and quality of eating	Awad and Waheedi[34]
		Improvement of obesity information and counseling skills of pharmacists and patient's cognition about ability of pharmacists for communication	
Doctors	USA	Review of patient progress with information for motivation	Patel[1]
		Adherence of the labeling recommendations regarding when and how to discontinue therapy	
		Specific attention to the weight-gaining properties of medications used to treat comorbid conditions	
		Review of patient progress with information for motivation	Patel[1]
		Provision of knowledge of weight-beneficial medications for specific diseases	Huang *et al.*[37] and Bleich *et al.*[38]
	Australia	Assessment of patient's dietary and physical activity habits	Campbell *et al.*[35]
		Provision of dietary and physical activity advice	
Nurses	UK	Provision of helpful care for weight control and management	Hoppe and Ogden[40]
		Key role in managing obesity	
		Provision of weight related interventions in primary care	Hoppe and Ogden[40] Zhu *et al.*[42]
		Provision of assistance with patients through counseling	Brown *et al.*[41]
		Training and organizational support for obesity management	Brown *et al.*[41] and Zhu *et al.*[42]

Roles of doctors: Doctors can contribute to reduce the obesity epidemic by adopting pharmacotherapies that meet consumer's needs, comorbidities and drug safety criteria. Doctors should inform patients when and how to cease therapy if weight loss is not achieved or if side effects outweigh drug benefits. In USA, doctors provide information on effective drugs for weight loss and help to manage obese patients with a comorbid status[1]. It is important that patients are provided with accurate information about obesity and the opportunity to lose weight with the assistance of doctors[38]. To prevent and treat obesity, advice from doctors is important for obese patients[38]. If a chronic care model is adapted to treat obesity, it is expected to facilitate effective treatment and provide patients with scientific information suitable for the management of obesity[55]. Doctors can encourage obese patients to lose weight through counseling[39]. In Australia, doctors check and counsel patients about lifestyles and dietary habits. While many efficient ways have been developed to address obesity, doctors did not consider obesity treatment as their roles[35]. However, in UK, although doctors considered their advice useless, they were found to be critical for the treatment of obesity[36].

Roles of nurses: In UK, nurses involved in primary care also participate in interventions targeting obesity[40,42]. To conduct intervention efficiently, it has been suggested that there is a need to develop an education program for nurses and to inform nurses and patients that self-assessment is important for treating obesity[40]. According to a study conducted in the UK, Chinese nurses conduct weight management programs better than English nurses[42]. Also, nurses who display confidence and a proper attitude when conducted weight counseling provide patients with organizational assistance[41]. It is important that patients consider interventions through nurses important for weight control and management[40]. To support nurses who are familiar with skills required for successful intervention, there are needs to establish standardized guidelines for obesity-related care, educate nurses to treat obesity properly and encourage nurses to provide appropriate intervention[41,42].

Systematic programs against anorectics: There is a need for efficient educational programs to prevent the abuse of anorectic drugs by obese patients.

As obesity has increased among children, the Centers for Disease Control (CDC) and other related authorities have promoted increasing time spent on physical activities to prevent obesity[56,57]. Web-based programs are more efficient for teens with respect to changing dietary habits and health conditions[58,59] and nutrition-related education is needed to encourage obese adults to consume more fruits and vegetables[60]. Also, there is a need to prepare programs for the illiterate and individuals with a poor educational background, because in one Iranian study it was found educational levels were related to obesity[61]. Some programs for health promotion are important for mothers to provide them with information about the risk of stillbirth, which is strongly related to maternal obesity and to encourage them to increase physical activity levels and take measures to prevent their children from becoming obese[62-64]. In USA, community based nutritional intervention programs have been reported to improve female health and reduce waist circumferences and depression[65].

CONCLUSION

The misuse and abuse of anorectic drugs have resulted in their side effects. Several prescription drugs, over-the-counter drugs and non-drug supplements are used to treat obesity. This narrative review focused on drugs likely to be misused and abused and it is evident that to prevent misuse and abuse problems, the roles of health professionals are important. Therefore, health providers should make efforts to ensure the appropriate use of anorectic drugs. Also, every health professionals should pay attention to health condition of patients and need to be well informed of obesity for provision of adequate treatment. Pharmacists should provide weight management and lifestyle interventions and provide dietary advice for successful weight management and provide information on meal replacement products and herbal products and on weight-beneficial medications for specific diseases. In addition, doctors and nurses should provide weight-related interventions to manage obesity.

To minimize and prevent problems resulting from the misuse and abuse of anorectic drugs, there is a need to develop and improve institutional and educational programs. On-line or in-person nutritional education or intervention would teach people to prevent obesity or manage themselves properly and appropriate health promotion programs would raise mother's perceptions regarding the management of obesity in their children.

It is still deficient for health professionals to pay attention to the abuse of anorectics, though they did the best they could. Therefore, this narrative review will be helpful for health professionals to make efforts to solve serious problems from abuse of anorectics.

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