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Obesity: Modern Medicine vs. Lifestyle

Jenny Christianson
University of North Dakota

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Jenny Christianson, PA-S
Department of Physician Assistant Studies, University of North Dakota School of Medicine & Health Sciences
Grand Forks, ND 58202-9037

UND School of Medicine & Health Sciences
University of North Dakota

Abstract

- *Obesity is a rising epidemic, and is one of the most common, costly and preventable health problems the world is experiencing today (Center for Disease Control and Prevention, [CDC], 2017).*
- From this, it is important to establish an effective treatment plan that can be implemented across the nation for maximum patient benefit.
- Lifestyle changes such as diet and exercise are important to any health care plan and are equally necessary to reduce health risks. However, in certain patients, lifestyle changes are not enough due to the maladaptive biologic process in their brain. Thus, additional treatment options need to be available to these patients.
- Both medical therapies, pharmacological and surgical, were found to be beneficial in augmenting lifestyle changes in multiple studies. Therefore, it was concluded that pharmacologic and surgical therapies are valid options in resistant obesity in addition to lifestyle changes such as diet and exercise.
- This study was a systematic literature review which evaluated studies from CINAHL, Clinical Key, Cochrane Library, and PubMed to formulate a conclusion. Research focused on two pharmacotherapy options, phentermine and orlistat, in addition to two surgical options, gastric bypass and sleeve gastrectomy, for added weight loss treatment when compared to lifestyle alone.

Introduction

- *Adulthood obesity is one of the most common, costly and preventable diseases the world is experiencing today (Center for Disease Control and Prevention, [CDC], 2017).*
- While obesity can be related to socioeconomic status and race, it is ultimately nondiscriminatory. Roughly 40% of Americans were obese as of 2016, whereas only 30% were in 2000 (National Center for Health Statistics, [NCHS], 2017).
- From this statistic it can be extrapolated that 32.75 million more Americans were diagnosed with obesity in 16 years, or **3-4 people every minute.**
- The purpose of this study is to determine the most effective treatment method available today to combat this rising epidemic.

Statement of the Problem

Obesity has a multitude of comorbidities associated with it such as: HTN, hyperlipidemia, diabetes mellitus type 2, stroke, coronary artery disease, depression and others, including death. Therefore, it is important to evaluate studies regarding each treatment method's effectiveness and long-term outcomes to better assess where more research should take place.

Research Questions

- In obese populations, Body Mass Index (BMI) greater than or equal to 30, do drug therapies, such as **phentermine** and **orlistat**, provide better long-term health outcomes than lifestyle changes to diet and exercise patterns?
- In obese populations, BMI greater than or equal to 30, do surgeries, such as **gastric bypass** and **sleeve gastrectomy** (SG), provide better long-term health outcomes than lifestyle changes to diet and exercise patterns?

Literature Review

- Alter et al. (2012) examined the cost of obesity on the Canadian health care system over 11.5 years. Obese individuals averaged about **$8,294.67 per person** when they had no other health related comorbidities, whereas their propensity matched normal weight counterparts costed **$7,323.59** (*p*=0.27). When **one negative health risk factor** was added to an obese individual their additional cost rose to **$2000 greater than their normal weight counterparts** with similar comorbidities. When **multiple risk factors** were present, obese individuals cost increased **$2700-$7000**.
- Moldovan et al. (2016) performed a highly controlled study where participants were given Medifast meal replacements and instructed to follow the Take Shape for Life Optimal Weight 5&1 Plan for weight loss and the *Habits of Health* program. There was a placebo group (no medication) and a phentermine HCl 37.5mg group. The **phentermine group experienced a more substantial fat and sweet craving decrease (*p*=0.012 and 0.038)**. Participants in the phentermine group also yielded **greater weight loss and BMI reduction** with 12.1% weight loss when compared to the placebo group with an 8.8% weight loss (*p*=0.028). Specifically, phentermine participants lost 2.1% more fat than the placebo group with a *p* value of 0.019.
- Samp, Al-Tahami, Ariffin, Omar, and Rasool (2015) evaluated a 9-month study where patients were on orlistat 120 mg three times a day, and then reevaluated the patients again 4 months after cessation of orlistat by anthropometric parameters. Nine-months of **orlistat treatment resulted in statistically significant decreases in total body weight, BMI, waist circumference, body and visceral fat percentage, total cholesterol, triglyceride, insulin levels and insulin resistance. *There was continued cardiovascular benefit 4 months after cessation of orlistat.***
- Foschi et al. (2018) evaluated an ileal interposition with duodenal diversion sleeve gastrectomy (II-DD-SG) to standard medical care in type two diabetic patients. **II-DD-SG's mean fasting plasma glucose (FPG) fell from 154.6 ± 6.4 to 89.6 ± 2.4 mg/dL and mean HbA1c from 7.7 ± 0.1% to 5.6 ± 0.2%** six months after surgery. These results were stable throughout the five years of the study with $p < 0.0001$. In **86% of the surgical patients** there was **complete diabetic remission** and **56% had remission of cardiovascular risk factors**. *Only two patients in the standard medical care group achieved complete remission of diabetes with no cardiovascular risk factor change.*
- Chopra, Chao, Etkin, Merklinger, Lieb, and Delany (2011) also evaluated SG and its effects on health status. Chopra was able to find that **84%** of their population had **improvement in diabetic status, 49.99%** had **improvement in hypertension control**, **90%** had **better asthma control**, **90.74%** found **improvements in** their **obstructive sleep apnea** symptoms, and **45.92%** had **better control** of their **gastroesophageal reflux disease**.
- Brandt, Clemensen, Nielsen, and Søndergaard (2018) found that **30% of participants initiated a lifestyle change because their healthcare provider voiced concern about their health.** Participants in this study also found it most effective to **continue lifestyle changes when their healthcare professional showed interest in their self-measurements and when they made more achievable daily goals.**
- Shaw, Gennat, O'Rourke, and Del Mar (2006) of Cochrane systematic review found that **exercise and diet combined, produced greater weight loss than exercise alone**, with a weighted mean difference (WMD) of 1.0 kg and a confidence interval (CI) of 95%. **Weight loss was also increased with increased intensity of exercise**, WMD 1.5 kg and CI 95% (Shaw et al., 2006). **Exercise also reduced diastolic blood pressure** by an average of 2 mmHg with a 95% CI**, reduced triglycerides** by 0.2 mmol/L with a 95% CI, **and fasting serum glucose** was found to have higher decreases with higher intensity workouts with a 0.3 mmol/L reduction and a 95%. Additionally, ***150 minutes of moderate exercise was shown to prevent weight gain, and 250 minutes or greater produced significant weight loss.***

Discussion

- Pharmacotherapies such as phentermine and orlistat, and weight loss surgeries such as gastric bypass and sleeve gastrectomy are valuable tools to treat obesity. They show increased weight loss results, and this helps patients to continue their weight loss efforts.
- However, all medical therapies come with risks. Therefore, all patients should be evaluated prior to starting any pharmacotherapy or surgical treatment.
- Additionally, weight loss will not be effective at reducing patient health risks without the adoption of lifestyle changes. Thus, in addition to evaluating for health contraindications, patients should be educated on lifestyle changes and show that they have incorporated these into their life before medical therapies should be initiated.
- As a clinician, it is imperative to provide support resources for the patient's weight loss journey with extensive follow up to encourage continued efforts.
- With these efforts on the patient and clinician's behalf, it may be possible to increase success rates in the treatment of obesity.

	Placebo	Phentermine 7·5 mg plus topiramate 46·0 mg	p value	Phentermine 15·0 mg plus topiramate 92·0 mg	p value
Waist circumference (cm)	−2·4 (−3·0 to −1·8); n=979	−7·6 (−8·4 to −6·9); n=488	<0·0001	−9·2 (−9·8 to −8·6); n=981	<0·0001
Systolic blood pressure (mm Hg)	−2·4 (−3·3 to −1·5); n=979	−4·7 (−5·9 to −3·5); n=488	0·0008	−5·6 (−6·5 to −4·6); n=980	<0·0001
Diastolic blood pressure (mm Hg)	−2·7 (−3·3 to −2·1); n=979	−3·4 (−4·2 to −2·6); n=488	0·1281	−3·8 (−4·4 to −3·2); n=980	0·0031
Total cholesterol (%)	−3·3 (−4·4 to −2·3); n=941	−4·9 (−6·3 to −3·6); n=475	0·0345	−6·3 (−7·4 to −5·3); n=964	<0·0001
LDL cholesterol (%)	−4·1 (−5·8 to −2·4); n=936	−3·7 (−6·0 to −1·5); n=475	0·7391	−6·9 (−8·6 to −5·2); n=961	0·0069
HDL cholesterol (%)	1·2 (−0·1 to 2·5); n=941	5·2 (3·5 to 6·9); n=475	<0·0001	6·8 (5·5 to 8·1); n=964	<0·0001
Triglycerides (%)	4·7 (1·4 to 8·0); n=941	−8·6 (−12·9 to −4·2); n=475	<0·0001	−10·6 (−13·9 to −7·3); n=964	<0·0001
Fasting glucose (mmol/L)	0·13 (0·06 to 0·19); n=938	−0·01 (−0·09 to 0·08); n=473	0·0047	−0·07 (−0·14 to −0·01); n=954	<0·0001
Glycated haemoglobin (%)	0·1 (0 to 0·1); n=805	0 (−0·1 to 0); n=449	<0·0001	−0·1 (−0·1 to 0); n=895	<0·0001
Fasting insulin (pmol/L)	5·1 (−6·0 to 16·3); n=925	−24·0 (−38·6 to −9·3); n=464	0·0004	−27·6 (−38·7 to −16·6); n=937	<0·0001
HOMA-IR	0·46 (−0·09 to 1·02); n=925	−0·93 (−1·67 to −0·20); n=464	0·0007	−1·07 (−1·62 to −0·52); n=937	<0·0001
hsCRP (mg/L)	−0·79 (−1·32 to −0·26); n=779	−2·49 (−3·17 to −1·81); n=440	<0·0001	−2·49 (−3·00 to −1·97); n=880	<0·0001
Adiponectin (µg/mL)	0·33 (0·11 to 0·56); n=737	1·40 (1·12 to 1·68); n=419	<0·0001	2·08 (1·87 to 2·29); n=836	<0·0001

Data are least-squares means (95% CI) derived from the intention-to-treat analysis with last observation carried forward, unless otherwise indicated. hsCRP=high-sensitivity C-reactive protein. HOMA-IR=homoeostasis model assessment-insulin resistance, calculated as (fasting glucose in mmol/L × fasting insulin in µIU/mL)/22·5. p values are for comparison of phentermine plus topiramate with placebo.

Table 2: Changes from baseline to week 56 in secondary endpoints

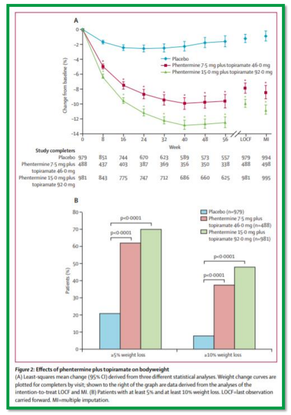
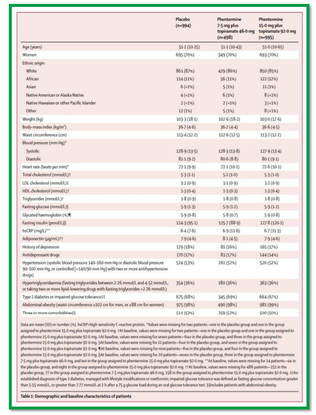


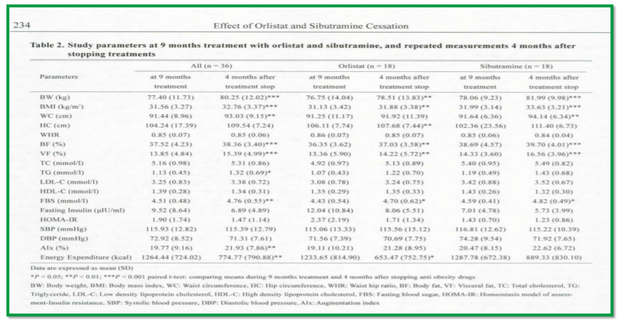
Figure 2: Effects of phentermine plus topiramate on bodyweight
(A) Least-squares mean change (95% CI) derived from three different statistical analyses. Weight change curves are plotted for completers by visit, shown to the right of the graph are data derived from the analyses of the intention-to-treat LOCF and MI. (B) Patients with at least 5% and at least 10% weight loss. LOCF=last observation carried forward. MI=multiple imputation.



	Placebo (n=994)	Phentermine 7·5 mg plus topiramate 46·0 mg (n=497)	Phentermine 15·0 mg plus topiramate 92·0 mg (n=992)
Age (years)	52·3 (10·25)	52·1 (10·43)	52·6 (10·55)
Women	695 (70%)	349 (70%)	691 (70%)
Ethnic origin			
White	861 (87%)	429 (86%)	850 (86%)
African	114 (11%)	58 (12%)	122 (12%)
Asian	8 (<1%)	5 (1%)	10 (1%)
Native American or Alaska Native	4 (<1%)	0 (%)	8 (<1%)
Native Hawaiian or other Pacific Islander	2 (<1%)	2 (<1%)	3 (<1%)
Other	12 (1%)	5 (1%)	8 (<1%)
Weight (kg)	103·1 (18·1)	103·6 (18·3)	103·0 (17·9)
Body-mass index (kg/m²)	36·7 (4·9)	36·9 (4·8)	36·6 (4·9)
Waist circumference (cm)	113·4 (12·7)	113·4 (12·5)	113·3 (12·7)
Blood pressure (mm Hg)*			
Systolic	128·9 (13·5)	128·3 (13·9)	127·9 (13·4)
Diastolic	81·5 (9·2)	80·6 (9·3)	81·1 (9·1)
Heart rate (beats per min)*	72·5 (9·9)	72·1 (10·1)	72·6 (10·1)
Total cholesterol (mmol/L)†	5·3 (1·1)	5·3 (1·0)	5·3 (1·1)
LDL cholesterol (mmol/L)†	3·2 (0·9)	3·1 (0·9)	3·2 (0·9)
HDL cholesterol (mmol/L)†	1·3 (0·4)	1·3 (0·3)	1·3 (0·4)
Triglycerides (mmol/L)†	1·8 (1·0)	1·8 (1·0)	1·8 (1·0)
Fasting glucose (mmol/L)‡	5·9 (1·3)	5·9 (1·2)	5·9 (1·2)
Glycated haemoglobin (%)¶	5·9 (0·8)	5·8 (0·7)	5·9 (0·8)
Fasting insulin (pmol/L)‖	134 (105·5)	135·7 (88·6)	127·8 (110·5)
hsCRP (mg/L)**	8·4 (7·6)	8·9 (11·6)	8·7 (10·3)
Adiponectin (µg/mL)††	7·9 (4·9)	8·1 (4·5)	7·9 (4·9)
History of depression	179 (18%)	85 (17%)	185 (19%)
Antidepressant drugs	170 (17%)	81 (17%)	166 (16%)
Hypertension (systolic blood pressure 140–160 mm Hg or diastolic blood pressure 90–100 mm Hg, or controlled [<140/90 mm Hg] with two or more antihypertensive drugs)	524 (53%)	261 (52%)	539 (52%)
Hypertriglyceridaemia (fasting triglycerides between 2·26 mmol/L and 4·52 mmol/L, or taking two or more lipid-lowering drugs with fasting triglycerides <2·26 mmol/L)	354 (36%)	189 (39%)	353 (34%)
Type 2 diabetes or impaired glucose tolerance‡‡	675 (68%)	345 (69%)	664 (67%)
Abdominal obesity (waist circumference ≥102 cm for men, or ≥88 cm for women)	975 (98%)	490 (98%)	981 (99%)
Three or more comorbidities§§	514 (52%)	258 (52%)	504 (51%)

Data are mean (SD) or number (%). hsCRP=high-sensitivity C-reactive protein. *Values were missing for two patients—one in the placebo group and one in the group assigned to phentermine 15·0 mg plus topiramate 92·0 mg. †At baseline, values were missing for two patients—one in the placebo group and one in the group assigned to phentermine 15·0 mg plus topiramate 92·0 mg. ‡At baseline, values were missing for seven patients—five in the placebo group, and three in the group assigned to phentermine 15·0 mg plus topiramate 92·0 mg. §At baseline, values were missing for 12 patients—four in the placebo group, and seven in the group assigned to phentermine 15·0 mg plus topiramate 92·0 mg. ¶At baseline, values were missing for nine patients—five in the placebo group, and four in the group assigned to phentermine 15·0 mg plus topiramate 92·0 mg. ‖At baseline, values were missing for 15 patients—seven in the placebo group, three in the group assigned to phentermine 7·5 mg plus topiramate 46·0 mg, and five in the group assigned to phentermine 15·0 mg plus topiramate 92·0 mg. **At baseline, values were missing for 14 patients—six in the placebo group, two in the group assigned to phentermine 7·5 mg plus topiramate 46·0 mg, and six in the group assigned to phentermine 15·0 mg plus topiramate 92·0 mg. ††At baseline, values were missing for 14 patients—six in the placebo group, three in the group assigned to phentermine 7·5 mg plus topiramate 46·0 mg, and five in the group assigned to phentermine 15·0 mg plus topiramate 92·0 mg. ‡‡At baseline, data were missing for 14 patients—six in the placebo group, two in the group assigned to phentermine 7·5 mg plus topiramate 46·0 mg, and six in the group assigned to phentermine 15·0 mg plus topiramate 92·0 mg. Only established diagnosis of type 2 diabetes, managed with lifestyle modifications or metformin; impaired glucose tolerance was defined as fasting glucose concentration greater than 5·55 mmol/L or greater than 7·77 mmol/L at 1 h after a 75 g glucose load during an oral glucose tolerance test. §§Includes patients with abdominal obesity.

Table 1: Demographic and baseline characteristics of patients



234 Effect of Orlistat and Sibutramine Cessation

Table 2. Study parameters at 9 months treatment with orlistat and sibutramine, and repeated measurements 4 months after stopping treatments

Parameters	All (n = 36)		Orlistat (n = 18)		Sibutramine (n = 18)	
	at 9 months treatment	4 months after treatment stop	at 9 months treatment	4 months after treatment stop	at 9 months treatment	4 months after treatment stop
BW (kg)	77.40 (11.73)	80.25 (12.02)***	76.75 (14.04)	78.51 (13.83)**	78.06 (9.23)	81.99 (9.98)***
BMI (kg/m²)	31.56 (3.27)	32.76 (3.37)***	31.13 (3.42)	31.88 (3.38)**	31.99 (3.14)	33.63 (3.21)***
WC (cm)	91.44 (8.96)	93.03 (9.15)**	91.25 (11.17)	91.92 (11.39)	91.64 (6.36)	94.14 (6.34)**
HC (cm)	104.24 (17.39)	109.54 (7.24)	106.11 (7.74)	107.68 (7.44)**	102.36 (23.56)	111.40 (6.73)
WHR	0.85 (0.07)	0.85 (0.06)	0.86 (0.07)	0.85 (0.07)	0.85 (0.06)	0.84 (0.04)
BF (%)	37.52 (4.23)	38.36 (3.40)***	36.37 (3.62)	37.03 (3.58)**	38.69 (4.37)	39.70 (4.01)***
VF (%)	13.85 (4.84)	15.39 (4.99)***	13.36 (5.90)	14.22 (5.72)**	14.33 (3.60)	16.56 (3.96)***
TC (mmol/l)	5.16 (0.98)	5.31 (0.86)	4.92 (0.97)	5.13 (0.89)	5.40 (0.95)	5.49 (0.82)
TG (mmol/l)	1.13 (0.47)	1.32 (0.69)*	1.07 (0.43)	1.22 (0.70)	1.19 (0.49)	1.43 (0.68)
LDL-C (mmol/l)	3.25 (0.83)	3.38 (0.72)	3.08 (0.78)	3.24 (0.75)	3.42 (0.88)	3.52 (0.67)
HDL-C (mmol/l)	1.39 (0.28)	1.34 (0.31)	1.35 (0.29)	1.35 (0.33)	1.43 (0.26)	1.32 (0.30)
FBS (mmol/l)	4.51 (0.48)	4.76 (0.53)**	4.43 (0.54)	4.70 (0.62)*	4.59 (0.41)	4.82 (0.49)*
Fasting Insulin (µIU/ml)	9.52 (8.64)	6.89 (4.89)	12.04 (10.84)	8.06 (5.51)	7.01 (4.78)	5.73 (3.99)
HOMA-IR	1.90 (1.74)	1.47 (1.14)	2.37 (2.19)	1.71 (1.34)	1.43 (0.70)	1.23 (0.86)
SBP (mmHg)	115.93 (12.82)	115.39 (12.79)	115.06 (13.33)	115.56 (15.12)	116.81 (12.62)	115.22 (10.39)
DBP (mmHg)	72.92 (8.52)	71.31 (7.61)	71.56 (7.39)	70.69 (7.75)	74.28 (9.54)	71.92 (7.65)
AIx (%)	19.77 (9.16)	21.93 (7.86)**	19.11 (10.21)	21.28 (8.95)	20.47 (8.15)	22.62 (6.72)
Energy Expenditure (kcal)	1264.44 (724.02)	774.77 (790.88)**	1233.65 (814.90)	653.47 (752.75)*	1287.78 (672.38)	889.33 (830.10)

Data are expressed as mean (SD)
*P < 0.05, **P < 0.01, ***P < 0.001 paired t-test: comparing means during 9 months treatment and 4 months after stopping anti obesity drugs
BW: Body weight, BMI: Body mass index, WC: Waist circumference, HC: Hip circumference, WHR: Waist hip ratio, BF: Body fat, VF: Visceral fat, TC: Total cholesterol, TG: Triglyceride, LDL-C: Low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol, FBS: Fasting blood sugar, HOMA-IR: Homeostasis model of assessment-Insulin resistance, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, AIx: Augmentation index

Applicability to Clinical Practice

- ✓ With the information provided in this systematic literature review, the clinician should be better able to address obese patient's treatment plans and give valuable information to the patient regarding their long-term weight loss outcomes with each method provided.
- ✓ Encouraging patients to work on **diet and exercise** for weight loss **should be integral to every treatment plan.**
- ✓ *However, if the patient does not exhibit results from this method*, pharmacological or surgical therapies should be tried based on the patient's individual health status, comorbidities, and benefit to risk ratios.

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UND School of Medicine & Health Sciences
University of North Dakota