UNIVERSITI SAINS MALAYSIA
GERAN PENYELIDIKAN UNIVERSITI
PENYELIDIKAN
LAPORAN AKHIR

OBESITY INTERVENTION OUTCOME: I)THE EFFECT OF PHARMACOLOGICAL INTERVENTION IN FAILED LIFESTYLE INTERVENTION II)WEIGHT LOSS MAINTENANCE WITH CESSATION OF PHARMACOLOGICAL INTERVENTION

PENYELIDIK

PROFESOR DR. AIDA HANUM GHULAM RASOOL

PENYELIDIK BERSAMA

PROFESSOR ABD AZIZ AL-SAFI ISMAIL
FARAH DIANA ARIFFIN

2013

UNIVERSITI SAINS MALAYSIA

BAHAGIAN PENYELIDIKAN
Pusat Pengajian Sains Perubatan

SENARAI SEMAKAN UNTUK BUKU LAPORAN AKHIR GERAN USM JANGKA PENDEK
(untuk di isi oleh penyelidik)

NAMA PENYELIDIK UTAMA	:	PROFESOR DR AIDA HANUM GHULAM RASOOL
NAMA CO-RESEARCHER	:	Profesor Abd. Aziz al-Safi Ismail Farah Diana Ariffin
TAJUK GERAN	:	Obesity Intervention Outcome: 1) The effect of pharmacological intervention in failed lifestyle intervention ii) weight maintenance with cessation of pharmacological intervention
NO.AKAUN		304/PPSP/6139072

SENARAI SEMAKAN SEMASA PENYERAHAN BUKU LAPORAN AKHIR
(Sila Tandakan (√) Pada Kotak Yang Berkenaan)

NO	PERKARA	ADA	TIADA
1.	**Borang Laporan Akhir Projek Penyelidikan USM Jangka Pendek**	/	
2.	**Borang Laporan Hasil Penyelidikan, PPSP**	/	
3.	**i) Salinan Menuskrip dan Salinan surat/email bukti penghantaran dan penerimaan manuskrip oleh mana-mana journal atau**	/	
	ii)Kertas penerbitan disertakan	/	
4.	**Penyata Perbelanjaan (Financial Statement)** **(Sila dapatkan daripada Jabatan Bendahari)**	/	
5.	**Laporan Komprehensif (termasuk kertas persidangan atau seminar dan penerbitan saintifik hasil daripada projek ini)**	/	
6.	**Surat pemakluman penghantaran Laporan Akhir ke Bhg. Penyelidikan**	/	

Nota:

1) **Sila buat 2 salinan buku laporan Akhir**
2) **No. 1- 5 - Perlu dimasukkan dalam Buku Laporan Akhir**
3) **No. 6 - Hantar terus Kepada Cik Noor Adnie Bajuri (RCMO) hanya salinan sahaja kepada Bhg. R&D, PPSP**

LAPORAN AKHIR PROJEK PENYELIDIKAN JANGKA PENDEK

FINAL REPORT OF SHORT TERM RESEARCH PROJECT

Sila kemukakan **dua (2) salinan** laporan akhir ini melalui Jawatankuasa Penyelidikan di Pusat Pengajian dan Dekan/ Pengarah/ Ketua Jabatan kepada Pejabat Pengurusan dan Kreativiti Penyelidikan (RCMO)

1. Nama Ketua Penyelidik: PROFESOR AIDA HANUM GHULAM RASOOL

☐ Profesor Madya/ *Assoc. Prof.* ☐ Dr./ *Dr.* ☐ Encik/Puan/Cik *Mr/Mrs/Ms*

2. Pusat Tanggungjawab (PTJ): Pusat Pengajian Sains Perubatan

3. Nama Penyelidik Bersama: Profesor Abdul Aziz al-Safi Ismail
Farah Diana Ariffin

4. Tajuk Projek: Obesity intervention outcome:
i) The effect of pharmacological intervention in failed lifestyle intervention,
ii) Weight loss maintenance with cessation of pharmacological intervention

5. Ringkasan Penilaian/*Summary of Assessment:*	**Tidak Mencukupi** *Inadequate* 1	2	**Boleh Diterima** *Acceptable* 3	**Sangat Baik** *Very Good* 4	5
i) Pencapaian objektif projek: *Achievement of project objectives*	☐	☐	☐	☐	☑
ii) Kualiti output: *Quality of outputs*	☐	☐	☐	☑	☐
iii) Kualiti impak: *Quality of impacts*	☐	☐	☐	☑	☐
iv) Pemindahan teknologi/potensi pengkomersialan: (NA) *Technology transfer/commercialization potential*	☐	☐	☐	☐	☐
v) Kualiti dan usahasama : (NA) *Quality and intensity of collaboration*	☐	☐	☐	☐	☐
vi) Penilaian kepentingan secara keseluruhan: *Overall assessment of benefits*	☐	☐	☐	☑	☐

6. **Abstrak Penyelidikan**
(Perlu disediakan di antara 100 - 200 perkataan di dalam **Bahasa Malaysia dan juga Bahasa Inggeris.** Abstrak ini akan dimuatkan dalam Laporan Tahunan Bahagian Penyelidikan & Inovasi sebagai satu cara untuk menyampaikan dapatan projek tuan/puan kepada pihak Universiti & masyarakat luar).

LAMPIRAN A

7. **Sila sediakan laporan teknikal lengkap yang menerangkan keseluruhan projek ini.**
[Sila gunakan kertas berasingan]

LAMPIRAN B

Senaraikan kata kunci yang mencerminkan penyelidikan anda:

Bahasa Malaysia	*Bahasa Inggeris*
Obesiti	obesity
Ubat anti-obesiti - orlistat dan sibutramin	anti-obesity drug treatment – orlistat & sibutramine

8. **Output dan Faedah Projek**

(a) * **Penerbitan Jurnal**
Publication of Journals
(Sila nyatakan jenis, tajuk, pengarang/editor, tahun terbitan dan di mana telah diterbit/diserahkan)
(State type, title, author/editor, publication year and where it has been published/submitted)

Accepted:

1. Effect of Orlistat and Sibutramine Cessation on Obesity Indices and Cardiovascular Risk Factors in Obese Subjects. Zulkefli Sanip, Belqes Al-Tahami, Farah Diana Ariffin, Noor Salwah O,Aida Hanum G Rasool. Tohoku Journal of Experimental Medicine. ISI indexed, impact factor = 1.244

2. Manuscript to be submitted to Malaysian Journal of Medicine and Health Sciences (draft attached). Effect of anti-obesity drug treatment in obese subjects who had failed to reduce weight via lifestyle Modification. Aida Hanum Ghulam Rasool, Farah Diana Ariffin, Abd. Aziz al-Safi, Noor Salwah Omar

(b) **Faedah-faedah lain seperti perkembangan produk, pengkomersialan produk/pendaftaran paten atau impak kepada dasar dan masyarakat.**

Implikasi amalan klinikal: Pemberhentian ubat anti-obesiti perlu disusuli dengan pemantauan yang berterusan dari segi aspek diet, peningkatan aktiviti fizikal. Sekiranya tidak, terbukti berat badan akan kembali menaik bersama dengan kemorosotan beberapa parameter risiko kardiovaskular dan metabolik. Ini mengurangkan faedah pemberian ubat obesiti itu sendiri.

Pengambilan ubat antiobesiti boleh menurunkan berat badan bagi mereka yang gagal menurunakan berat badan secara diet dan peningkatan aktiviti fizikal. Namun, tidak semestinya ianya disertai dengan faedah pengurangan risiko kardiovaskular dan metabolik – amalan gaya hidup sihat amat perlu untuk faedah kesihatan.

(c) **Latihan Sumber Manusia**

i) Pelajar Sarjana:
Graduates Students
(Perincikan nama, ijazah dan status):
(Provide names, degrees and status)

Projek di bantu oleh pelajar sarjana Farah Diana Ariffin dan pegawai sains

ii) Lain-lain:

Pembentangan kertas kerja peringkat Antarabangsa:

1) Aida Hanum G Rasool[1], Belqes AM Al-Tahami[1], Zulkefli Sanip[2], Farah Diana Ariffin[1], Noor Salwah Omar[3] Effect of Orlistat and Sibutramine Cessation on Obesity Indices and Cardiovascular Risk Factors in Obese Subjects. International Congress of Medical and Health Sciences, 2013

2) Aida Hanum G Rasool[1], Farah Diana A[1], AA al-Safi[2], Noor Salwah O[3] The Effect of Anti-Obesity Drugs on Weight Reduction and Cardiometabolic Markers in Failed Lifestyle Intervention. Int. Congress of Medical & Health Sciences, 2013

9. **Peralatan yang Telah Dibeli:**
Equipment that has been purchased **tiada**

Komen Jawatankuasa Penyelidikan Pusat Pengajian/Pusat
Comments by the Research Committees of Schools/Centres

Boleh diterima

Tutup Geran

24/8/13

BORANG LAPORAN HASIL PENYELIDIKAN
PPSP

Tajuk geran: Obesity intervention outcome:

i. The effect of pharmacological intervention in failed lifestyle intervention,
ii. Weight loss maintenance with cessation of pharmacological intervention

Penyelidik: Profesor Dr Aida Hanum Ghulam Rasool
Jenis geran: Jangka Pendek USM
Tempoh geran: 01 November 2009 – 30 April 2012

Jenis laporan: Laporan Kemajuan ☐ Alatan di beli ☐ Ya:nyatakan.....

Laporan Akhir*: ☑ ☑ Tidak

OBJEKTIF SPESIFIK KAJIAN (sama spt dalam proposal asal)	**SECARA RINGKAS TERANGKAN PENCAPAIAN/HASIL**	**OBJEKTIF TERCAPAI ATAU TIDAK**
To assess the effect of four months pharmacological intervention on weight loss in patients who had failed to achieve satisfactory weight loss via a monitored lifestyle modification programme	Orlistat and Sibutramine reduced weight significantly in subjects who had failed with education on lifestyle medication. The weight reduction was however modest at 3% and was not associated with improvements in measured cardiometabolic markers.	YA
To assess weight loss maintenance in subjects after stopping anti-obesity drug intervention	Orlistat and sibutramine cessation produced weight regain and increased certain obesity indices as early as 4 months after cessation. Continuous rigorous follow up and reinforcement is needed to ensure weight regain is prevented or minimized to maintain beneficial effects achieved with anti-obesity drug treatment.	YA

LAMPIRAN A

TAJUK PENYELIDIKAN:

HASIL INTERVENSI OBESITI;

1. **KESAN INTERVENSI FARMAKOLOGI DALAM KALANGAN YANG GAGAL INTERVENSI GAYA HIDUP**
2. **PENGEKALAN PENURUNAN BERAT BADAN DENGAN PEMBERHENTIAN INTERVENSI FARMAKOLOGI**

ABSTRAK 1

Kesan Intervensi Farmakologi dalam Kalangan yang Gagal Intervensi Gaya Hidup

Objektif: Kajian ini bertujuan menentukan kesan ubat anti-obesiti ke atas subjek obes yang gagal mencapai penurunan berat badan yang memuaskan selepas 9 bulan program mengurangkan berat badan secara pendidikan gaya hidup sihat.

Methods: 11 subjek (8 wanita dan 3 lelaki) yang telah melalui 9 bulan program intervensi bagi mengurangkan berat badan secara gaya hidup sihat dan masih gagal menurunkan berat badan secara memuaskan (didefinisikan sebagai masih mempunyai BMI > 27 kg/m2) telah ditawarkan pengambilan ubat anti-obesiti selama 4 bulan. Ukuran antropometrik, peratus lemak badan dan viseral, profil metabolik dan kardiovaskular (CVS) telah diukur pada 9 bulan selepas tamat gaya hidup sihat, dan 4 bulan selepas mengambil ubat anti-obesiti. Ubat yang digunakan dalam kajian ini samada orlistat 120 mg tiga kali sehari atau sibutramin 10-15 mg sekali sehari.

Results: 7 subjek telah menerima orlistat manakala 4 telah mengambil sibutramin. 11 subjek ini tidak menunjukkan penurunan berat badan yang signifikan semasa 9 bulan intervensi gaya hidup sihat, berat badan adalah 75.7 (18.8) dan 76.5 (21.0) kg masing-masing. Berat badan mereka selepas 4 bulan pengambilan ubat turun secara signifikan sebanyak 2.06 kg (p=0.041). Peratus lemak visceral telah turun secara signifikan daripada 13.7 (6.5) kepada 12.9 (6.9)%, (p=0.036), manakala kelihatan terdapat corak penurunan ukurlilit pinggang (87.2 (10.2) vs 85.9 (11.0) cm, p = 0.073). selepas 4 bulan pengambilan ubat. Tiada perbezaan dilihat pada profil lemak darah, paras gula puasa, paras insulin dan kerintangan insulin, tekanan darah dan ketegangan salurdarah selepas 4 bulan pengambilan ubat.

Kesimpulan: Orlistat and Sibutramin menurunkan berat badan secara signifikan dalam kalangan subjek yang gagal menurunkan berat badan dengan memuaskan selepas intervensi

pendidikan gaya hidup sihat. Walau bagaimanapun pengurangan berat badan adalah kecil pada paras 2.7%, dan ianya tidak disertai dengan penambahbaikan dari segi parameter kardiovaskular dan metabolik yang diukur.

ABSTRAK 2

Pengekalan Penurunan Berat Badan dengan Pemberhentian Intervensi Farmakologi

Objektif: Kesan pemberhentian ubat anti-obesiti ke atas profil antropometrik and risiko kardiovaskular (CVD) kurang diketahui dan dikaji. Tujuan kajian ini adalah untuk menilai kesan pemberhentian ubat anti-obesiti orlistat dan sibutramin selepas 9 bulan rawatan ke atas profil antropometrik dan risiko kardiovaskular.

Kaedah penyelidikan: 36 subjek obes yang telah melalui 9 bulan rawatan obesiti menggunakan orlistat dan sibutramin telah dipanggil balik 4 bulan selepas pemberhentian ubat-ubat tersebut. 18 subjek telah menerima 120 mg orlistat tiga kali sehari manakala 18 subjek telah menerima 10-15 mg sibutramin setiap hari. Profil antropometrik and metabolik, paras gula semasa puasa, paras insulin dan kerintangan insulin (HOMA-IR), tekanan darah, ketegangan salurdarah (dikuantifikasikan sebagai AI%) dan penggunaan tenaga diukur pada sebelum ubat diberhentikan pada 9 bulan rawatan, dan 4 bulan selepas ubat diberhentikan.

Keputusan: 4 bulan selepas pemberhentian ubat, terdapat peningkatan berat badan (80.25 vs 77.40 kg), BMI (32.76 vs 31.56 kg/m2), ukur lilit pinggan (93.03 vs 91.44 cm), peratus lemak badan (38.36 vs 37.52%), peratus lemak viseral (15.39 vs 13.85%), paras trigliserida (1.32 vs 1.13 mmol/l), paras gula berpuasa (4.76 vs 4.51 mmol/l) dan ketegangan salurdarah (21.93 vs 19.77%). Peningkatan balik berat badan adalah lebih kecil berbanding dengan yang turun semasa rawatan orlistat, tetapi lebih tinggi bagi rawatan sibutramin.

Kesimpulan: Peningkatan berat badan dan beberapa parameter berkait obesiti berlaku seawal 4 bulan selepas ubat anti-obesiti orlistat dan sibutramin diberhentikan. Pemantauan berterusan diperlukan selepas rawatan dengan ubat anti-obesiti bagi mengelak atau mengurangkan kenaikan semula berat badan bagi mengekalkan manfaat rawatan anti-obesiti.

ABSTRACT

Obesity intervention outcome:

i. **The effect of pharmacological intervention in failed lifestyle intervention,**

ii. **Weight loss maintenance with cessation of pharmacological intervention**

ABSTRACT 1

The Effect of Pharmacological Intervention in Failed Lifestyle Intervention

Objective: This study aimed to determine the effect of anti-obesity drug treatment in overweight and obese subjects who had failed to achieve satisfactory weight loss after a 9 months' weight loss intervention programme involving education on lifestyle modification.

Methods: 25 subjects had originally undergone a 9 months' intervention programme aimed to reduce weight involving education on lifestyle modification. 11 (8 females and 3 males) subjects who had failed to reduce their weight satisfactorily (defined as still having body mass index (BMI) $\geq$ 27 kg/m2 after intervention) were offered anti-obesity drugs for a period of 4 months. Anthropometric measurements, body composition (body and visceral fat percentages), metabolic and cardiovascular (CVS) profiles were measured at 9 months after completing lifestyle modification, and repeated at the end of 4 months with anti-obesity drugs. Anti-obesity drugs used in this study were orlistat 120 mg three times daily or sibutramine 10 – 15 mg daily.

Results: 7 subjects were on orlistat while 4 were on sibutramine. These 11 subjects did not significantly reduce weight when they were on 9 months education on lifestyle modification, mean weight before and after intervention was 75.7 (18.8) vs 76.5 (21.0) kg; p=0.452. Weight reduced significantly after 4 months drug treatment by 2.06 kg (p=0.041). Visceral fat significantly reduced from 13.7 (6.5) % to 12.9 (6.9) % (p=0.036) after drug treatment. A borderline reduction in waist circumference was seen (87.2 (10.2) cm vs 85.9 (11.0) cm, (p = 0.073). No difference was seen in lipid profile, fasting blood sugar, insulin level and resistance, blood pressure and arterial stiffness with 4 months anti-obesity agents.

Conclusion: Orlistat and Sibutramine reduced weight significantly in subjects who had failed to reduce weight with education on lifestyle medication. The weight reduction was however modest at 2.7% and was not associated with improvements in other CVS and metabolic risk markers.

ABSTRACT 2

Weight Loss Maintenance with Cessation of Pharmacological Intervention

Objective: The effects of ceasing anti-obesity drugs on anthropometric profile and cardiovascular risk have not been well studied. We aimed to evaluate the effects of orlistat and sibutramine cessation after a 9 months weight loss programme on anthropometric profile and cardiovascular risk factors.

Methods: 36 obese subjects who had undergone a 9 months weight loss programme with orlistat and sibutramine were followed up 4 months after ceasing the anti-obesity drugs. 18 subjects received 120 mg orlistat three times daily and 18 were on 10-15 mg sibutramine daily. Anthropometric and metabolic profiles, fasting blood sugar, insulin levels, insulin resistance (HOMA-IR), blood pressure, systemic arterial stiffness (quantified as central augmentation index) and energy expenditure were measured during 9 months treatment and 4 months after ceasing anti-obesity drugs.

Results: After cessation, there were significant increases in body weight (80.25 vs 77.40 kg), BMI (32.76 vs 31.56 kg/m2), waist circumference (93.03 vs 91.44 cm), body fat percentage (38.36 vs 37.52%), visceral fat percentage (15.39 vs 13.85%), triglyceride levels (1.32 vs 1.13 mmol/l), fasting blood sugar (4.76 vs 4.51 mmol/l) and systemic arterial stiffness (21.93 vs 19.77%). The magnitude of weight regain was smaller to that lost during orlistat treatment, but was higher in sibutramine-treated group.

Conclusion: Orlistat and sibutramine cessation produced weight regain and increased certain obesity indices as early as 4 months after cessation. Continuous rigorous follow up and reinforcement is needed to ensure weight regain is prevented or minimized to maintain beneficial effects achieved with anti-obesity drug treatment.

LAMPIRAN B

COMPREHENSIVE TECHNICAL REPORT

Research Objectives

1. To assess the effects of 4 months pharmacological intervention on weight loss in patients who had failed to achieve satisfactory weight loss via a monitored lifestyle modification programme (Study 1)

2. To assess weight loss maintenance in subjects after stopping anti-obesity drug intervention (Study 2)

Background

Prevalence of obesity among Malaysians are increasing. In Malaysia, the 2007 Malaysian NCD (non-communicable disease) Survey reported that in adult males, 30.9% were overweight while 13.9% were obese. For women, 32.4% were reported as overweight, while 18.8% were considered obese. This is a worrying trend, as obesity is associated with a number of health risks such as:

- Metabolic disorders such as diabetes, metabolic syndrome, dyslipidemia
- Cardiovascular diseases eg coronary artery diseases, stroke, hypertension
- Others eg orthopaedic, infertility

We have previously shown that obesity is associated with impaired microvascular endothelial function, which was associated with higher blood pressure, increased C-reactive protein and serum triglyceride and lower HDL-C cholesterol compared to non-obese controls (Balqes & Aida et al, 2009). Obesity increases CVS risks and complications, thus weight reduction will alter the early development of CVS risk thus becomes an important goal for obese patients. Weight loss in obese subjects has also been shown to reduce risk of getting diabetes in these subjects. Among the intervention methods used for weight loss in Malaysia are lifestyle modification in the form of caloric restriction and increased physical activity, and pharmacological management.

The 2 pharmacological agents commonly used in Malaysia as anti obesity agents are orlistat and sibutramine. Orlistat is a lipase inhibitor that prevents fat absorption thus facilitates weight loss. Sibutramine has combined noradrenaline and serotonin reuptake inhibitor properties. Sibutramine's effect on weight loss is attributed to appetite suppression and increased thermogenesis, secondary to stimulation of brown adipose tissue.

Basis for study 1:

Objective: To assess the effect of four months pharmacological intervention on weight loss in patients who had failed to achieve satisfactory weight loss via a monitored lifestyle modification programme

Lifestyle modification, with adjustments to dietary habits and increased physical activity is one intervention used to reduce weight. However, to achieve weight loss via this method, a lot

of determination and will power on the patients part is needed, which is not often achievable. This is especially so in some patients who have problems engaging in active physical activity such as those with orthopaedic problems, who frequently needs to use non steroidal anti inflammatory drugs. This has been noted in some of our patients who were previously on lifestyle modification and were not able to reduce much weight. We also noted a few of our patients whom, despite controlling their dietary habits and increasing physical activity, still failed to reduce their weight. There is actually a dearth of knowledge on the use of pharmacological intervention in patients who had failed a monitored lifestyle modification programme. Thus the aim of Part 1 of our project to determine weight reduction and cardiovascular risk reduction in these group of patients.

Basis for Study 2:

There are a few studies (mainly observational) looking at the maintenance of weight loss in groups who had been on lifestyle (mainly dietary) interventions (Anderson et al., 2001). However, there is a dearth of information on the effect of stopping pharmacological intervention to weight and other anthropometric measures. There is only one study that had assessed the effect of stopping orlistat after 6 months of intervention and following up patients for 6 months later (Woo et al., 2007). They had shown that weight had increased by approximately 2.5% in non diabetic subjects (n=13) while in the diabetics (n=15) weight has increased by approximately 3.9% if no active intervention was instituted. We could not find a study documenting effect on weight regain in subjects previously on sibutramine. Most literature reports on weight maintenance are performed to determine weight maintenance while patients are still on anti-obesity medication; thus the importance of this study. We need to have evidence on the outcome of weight reduction after cessation of treatment with anti-obesity medication. Thus the aim of this second part of our study is to determine whether weight reduced with anti-obesity medication for nine months is maintained after 4 months.

Obesity is associated with metabolically related CVS risk factors such as elevated blood pressure, hypercholesterolemia and hyperinsulinemia, thus changes in lipid profile, fasting glucose and insulin sensitivity will also be assessed in this study.

Methodology

Ethical approval for this study was obtained from the Human Ethical Committee of Universiti Sains Malaysia. Most subjects in this study were subjects from our previous obesity related research project.

This project consisted of 2 parts.

Study 1

A prospective intervention study that involved 11 subjects (8 females and 3 males). These subjects had earlier participated in a 9 months' study that involved education on lifestyle modification to reduce weight. These subjects had failed to reduce their weight satisfactorily (defined as still having body mass index (BMI) $\geq$ 27 kg/m2 after 9 months intervention). They were offered anti-obesity drugs for a period of 4 months. Anthropometric measurements, body composition (body and visceral fat percentages), metabolic and cardiovascular (CVS) profiles

were measured at 9 months after completing lifestyle modification, and repeated at the end of 4 months with anti-obesity drugs. Anti-obesity drugs used in this study were orlistat 120 mg three times daily or sibutramine 10 – 15 mg daily.

Study 2

36 obese subjects who had undergone a 9 months' weight loss programme with orlistat and sibutramine were followed up 4 months after ceasing their anti-obesity drugs. 18 subjects received 120 mg orlistat three times daily and 18 were on 10-15 mg sibutramine daily. Anthropometric and metabolic profiles, fasting blood sugar, insulin levels, insulin resistance (HOMA-IR), blood pressure, systemic arterial stiffness (quantified as central augmentation index) and energy expenditure were measured during 9 months drug treatment and 4 months after ceasing anti-obesity drugs.

Study inclusion and exclusion criteria.

Inclusion criteria:

1- Overweight male and female subjects above the age of 18 years who gave their informed consent to participate in this study.

2- Normotensive and controlled hypertensive (SBP<150 mmHg and DBP<100 mmHg).

Exclusion criteria:

1. History of coronary artery diseases (myocardial infarction, coronary bypass, heart failure, arrhythmia) or stroke.
2. Debilitating medical conditions which include liver failure, renal failure, and malignancy.
3. Diabetes
4. Pregnancy and lactating
5. Subjects receiving a monoamine oxidase inhibitor or selective serotonin reuptake inhibitor
6. History of major eating disorder such as anorexia, bulimia
7. History of active psychiatric illness and drug abuse

Study parameters:

1. Anthropometric measurements include weight, body mass index, waist circumference, waist hip ratio, percentage body fat
2. Arterial stiffness: Using parameters obtained from pulse wave analysis. These procedures were conducted non invasively using the equipment Sphygmocor.
3. Peripheral and central blood pressure
4. Metabolic markers: insulin sensitivity, lipid profile, fasting blood sugar

All subjects will also be asked to fill in the Paffenberger physical activity questionnaire before and after 4 months intervention (Montoye, 1996)

Statistical analysis
Statistical analysis was performed using the Statistical Package for the Social Sciences software version 18.0 package for Windows (SPSS Inc, 2009). Change in study parameters between baseline and 4 months follow up were analysed using paired t-test or the non parametric equivalent where required. Results are expressed as mean (standard deviation) and p value of less than 0.05 was considered statistically significant.

The Importance and the Benefits of the Research
Obesity is becoming an endemic problem in our community now. Obesity increases cardiovascular mortality and morbidity, besides having influence on other organ systems problems such as musculoskeletal, metabolic and reproductive. This research will look at the eventual outcome of pharmacological and non pharmacological interventions in obesity. This will help us generate information and evidence on obesity management that will help us in the management of obesity in our population.

RESULTS

Study 1:
Mean age of subjects in the study was 37.8 (7.7) years.
There were no significant differences in the mean weight of the 11 subjects in anthropometric variables, metabolic and hemodynamic profiles after 9 months education on lifestyle modification intervention. After 4 months on anti-obesity drugs, subjects showed a small but significant decrease in body weight (-2.1 kg) and visceral fat (-0.8) level and marginally significant decrease in waist circumference ($p=0.073$). No significant differences were detected in other anthropometric variables, metabolic and hemodynamic profiles after 4 months drug intervention (Table 1).

Study 2
9 months treatment with anti-obesity agents (which include orlistat and sibutramine) in these 36 subjects produced significant decreases in body weight, BMI, waist circumference, body and visceral fat percentage, total cholesterol, triglyceride, insulin level and insulin resistance (HOMA-IR). There was also significant increases in energy expenditure at the end of both orlistat and sibutramine treatment (Table 2).

After 4 months of stopping anti-obesity drug treatment, there were significant increases in body weight, BMI, waist circumference, body and visceral fat percentage, triglyceride, fasting blood sugar and central augmentation index. Energy expenditure was found to be significantly decreased after 4 months of stopping anti-obesity drug treatment (Table 2). Table 3 also showed changes in these parameters when they were subdivided into two groups based on their initial anti-obesity drug use; 18 patients who had stopped orlistat for four months, and 18 patients who had ceased from sibutramine. Body weight, BMI, hip circumference, body and visceral fat percentage and fasting blood sugar were significantly increased while energy expenditure was found to be significantly decreased in the orlistat-treated group 4 months after treatment completion. Sibutramine-treated group showed significant increases in body weight, BMI, waist

UNIVERSITI SAINS MALAYSIA
JABATAN BENDAHARI
KUMPULAN WANG PENYELIDIKAN GERAN USM(304)
PENYATA PERBELANJAAN SEHINGGA 31 MAC 2012

Jumlah Geran:	RM	39,996.00	Ketua Projek:	Aida Hanum Ghulam Rasool, Prof M.
Peruntukan 2009 (Tahun 1)	RM	24,130.00	Tajuk Projek:	Obesity Intervention Outcome:1) The Effect of Pharmacological Intervention in Failed Lifestyle Intervention ii) Weight Loss Maintenance with Cessation of Pharmacological Intervention
Peruntukan 2010 (Tahun 2)	RM	15,866.00		
			Tempoh:	01 Nov 2009- 31 Okt 2011 (LANJUT TEMPOH -1 NOV-30 APRIL 2012)
			No.Akaun:	304/PPSP/6139072

Kwg	Akaun	PTJ	Projek	Peruntukan Projek	Perbelanjaan T'kumpul Hingga Tahun Lalu	Peruntukan Semasa	Tanggungan Semasa	Bayaran Tahun Semasa	Belanja Tahun Semasa	Baki Projek
304	11000	PPSP	6139072	10,056.00	6,668.57	3,387.43	-	-	-	3,387.43
304	14000	PPSP	6139072	1,600.00	-	1,600.00	-	-	-	1,600.00
304	15000	PPSP	6139072	-	-	-	-	-	-	-
304	21000	PPSP	6139072	3,000.00	1,532.00	1,468.00	-	793.00	793.00	675.00
304	22000	PPSP	6139072	-	-	-	-	-	-	-
304	23000	PPSP	6139072	300.00	170.70	129.30	45.00	-	45.00	84.30
304	24000	PPSP	6139072	-	90.00	(90.00)	-	-	-	(90.00)
304	25000	PPSP	6139072	-	20.10	(20.10)	-	-	-	(20.10)
304	26000	PPSP	6139072	-	205.00	(205.00)	175.00	-	175.00	(380.00)
304	27000	PPSP	6139072	8,280.00	17,212.96	(8,932.96)	2,647.00	1,610.00	4,257.00	(13,189.96)
304	28000	PPSP	6139072	-	-	-	-	-	-	-
304	29000	PPSP	6139072	16,760.00	7,802.60	8,957.40	135.00	-	135.00	8,822.40
304	32000	PPSP	6139072	-	-	-	-	-	-	-
304	35000	PPSP	6139072	-	-	-	-	-	-	-
304	A11559	PPSP	6139072	-	-	-	-	-	-	-
304	A11102	PPSP	6139072	-	-	-	-	-	-	-
				39,996.00	33,701.93	6,294.07	3,002.00	2,403.00	5,405.00	889.07

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Effect of Orlistat and Sibutramine Cessation on Obesity Indices and Cardiovascular Risk Factors in Obese Subjects

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Abstract:	The effects of ceasing anti-obesity drugs on anthropometric profile and cardiovascular risk factors have not been well studied. We aimed to evaluate the effects of orlistat and sibutramine cessation after a 9 months weight loss programme on anthropometric profile and cardiovascular risk factors. 36 obese subjects who had undergone a 9 months weight loss programme with orlistat and sibutramine were followed up 4 months after ceasing the anti-obesity drugs. 18 subjects received 120 mg orlistat three times daily and 18 were on 10-15 mg sibutramine daily. Anthropometric and metabolic profiles, fasting blood sugar, insulin levels, insulin resistance (HOMA-IR), blood pressure, systemic arterial stiffness (quantified as central augmentation index) and energy expenditure were measured during 9 months treatment and 4 months after ceasing anti-obesity drugs. After cessation, there were significant increases in body weight (80.25 vs 77.40 kg), BMI (32.76 vs 31.56 kg/m2), waist circumference (93.03 vs 91.44 cm), body fat percentage (38.36 vs 37.52%), visceral fat percentage (15.39 vs 13.85%), triglyceride levels (1.32 vs 1.13 mmol/l), fasting blood sugar (4.76 vs 4.51 mmol/l) and systemic arterial stiffness (21.93 vs 19.77%). The magnitude of weight regain was smaller to that lost during orlistat treatment, but was higher in sibutramine-treated group. Orlistat and sibutramine cessation produced weight regain and increased certain obesity indices as early as 4 months after cessation. Continuous rigorous follow up is needed to ensure weight regain is prevented or minimized to maintain beneficial effects achieved with anti-obesity drug treatment.

Effect of Orlistat and Sibutramine Cessation on Obesity Indices and Cardiovascular Risk Factors in Obese Subjects

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Abstract

The effects of ceasing anti-obesity drugs on anthropometric profile and cardiovascular risk factors have not been well studied. We aimed to evaluate the effects of orlistat and sibutramine cessation after a 9 months weight loss programme on anthropometric profile and cardiovascular risk factors. 36 obese subjects who had undergone a 9 months weight loss programme with orlistat and sibutramine were followed up 4 months after ceasing the anti-obesity drugs. 18 subjects received 120 mg orlistat three times daily and 18 were on 10-15 mg sibutramine daily. Anthropometric and metabolic profiles, fasting blood sugar, insulin levels, insulin resistance (HOMA-IR), blood pressure, systemic arterial stiffness (quantified as central augmentation index) and energy expenditure were measured during 9 months treatment and 4 months after ceasing anti-obesity drugs. After cessation, there were significant increases in body weight (80.25 vs 77.40 kg), BMI (32.76 vs 31.56 kg/m^2), waist circumference (93.03 vs 91.44 cm), body fat percentage (38.36 vs 37.52%), visceral fat percentage (15.39 vs 13.85%), triglyceride levels (1.32 vs 1.13 mmol/l), fasting blood sugar (4.76 vs 4.51 mmol/l) and systemic arterial stiffness (21.93 vs 19.77%). The magnitude of weight regain was smaller to that lost during orlistat treatment, but was higher in sibutramine-treated group. Orlistat and sibutramine cessation produced weight regain and increased certain obesity indices as early as 4 months after cessation. Continuous rigorous follow up is needed to ensure weight regain is prevented or minimized to maintain beneficial effects achieved with anti-obesity drug treatment.

Keywords: Anti-obesity cessation, orlistat, sibutramine, obesity