UNIVERSITI PUTRA MALAYSIA

EFFECTS OF MEAL REPLACEMENT THERAPY ON BODY WEIGHT, GLYCEMIC CONTROL AND CARDIOVASCULAR DISEASE RISKS IN OBESE TYPE 2 DIABETES PATIENTS

GEW SOON PENG

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By

GEW SOON PENG

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Master of Science

March 2018
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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Master of Science

EFFECTS OF MEAL REPLACEMENT THERAPY ON BODY WEIGHT, GLYCEMIC CONTROL AND CARDIOVASCULAR DISEASE RISKS IN OBESE TYPE 2 DIABETES PATIENTS

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GEW SOON PENG

March 2018

Chair: Assoc. Prof. Barakatun Nisak Binti Mohd Yusof, PhD
Faculty: Medicine and Health Sciences

Obesity is a common presentation in patients with type 2 diabetes mellitus (T2DM). Reducing as little as 5% of body weight may assist in improving diabetes-related outcomes. While the use of meal replacement therapy (MRT) as part of the medical nutrition therapy (MNT) is recommended, its effectiveness remains unclear, especially in the Malaysian context. This study has evaluated the effect of MRT on body weight, glycemic control and cardiovascular disease (CVD) risks in obese patients with T2DM. Thirty-two (n = 32) obese participants with T2DM (mean; age = 46.4 ± 8.2 years old; female = 34.4%, body mass index (BMI) = 31.8 ± 4.9 kg/m²; glycated haemoglobin (HbA1c) = 8.8 ± 1.5%) were recruited from the National Diabetes Institute (NADI), Diabetes Resource Centre. Participants were randomised to either MRT (n = 16) or standard dietetic therapy (SDT) group (n = 16) for 12-weeks study. All of the participants received the MNT from a dietitian at Diabetes Resource Centre with iso-caloric prescriptions at 1200 kcal/day depending on their needs. Participants in the MRT group were asked to replace their two meals with the two meal replacements in a day, with a snack and healthy meal plan at dinner time. The SDT group was asked to consume three carbohydrate-controlled meal plan and a snack. The parameters of body weight, body composition, glycemic control and CVD risks were assessed at baseline, 6 and 12 weeks. The data presented based on intention-to-treat analysis. A total of 27 participants completed the study for an 84.4% response rate (MRT = 14, 87.5%; SDT = 13, 81.3%). The baseline characteristics were comparable between groups. At 12-weeks, the MRT group had a significantly large magnitude of changes (ηp² = 0.272, p = 0.010) and greater reduction in body weight (83.3 ± 13.0 kg, Δ baseline = -3.5 ± 0.5 kg) than the SDT group (87.2 ± 20.8 kg, Δ baseline = -1.1 ± 2.4 kg; p < 0.01). The percentage of weight loss in the MRT group (Δ baseline = -4.1 ± 2.1%) was significantly greater than the SDT group (Δ baseline = -1.4 ± 2.5%; p < 0.01). Significant improvements in BMI and body fat percentage were also observed in the MRT group as compared to the SDT group (p < 0.01). In general, the differences between groups on HbA1c
were not significant. However, the MRT group had a greater reduction in HbA1c and dosage of OAD as compared with the SDT group. HbA1c in the MRT group was reduced from 9.1 ± 1.5% to 7.9 ± 1.3% (Δ baseline = -1.1%; p < 0.01), which was not observed in the SDT group (baseline = 8.5 ± 1.5%; 12-weeks = 8.0 ± 1.1%; Δ baseline = -0.5%; p = 0.11). Fasting plasma glucose (FPG) also declined in the MRT group (Δ baseline = -1.2 ± 2.2 mmol/L; p < 0.05), but not in the SDT group, with no significant differences between groups. Interestingly, analysis of minimised confounders effects by removing the participants who had changed type of oral anti-diabetic drug (OAD) showed significant differences, with a large magnitude of changes (ηp² = 0.255, p = 0.006). Weight loss was associated with HbA1c reduction. CVD risks tended to improve more in the MRT group than in the SDT group, but no significant differences were found between the groups. 72.5% of the MRT participants adhered to the intervention. Adherence to MRT was associated with weight loss, visceral fat reduction, HbA1c reduction and high-sensitivity C-reactive protein (hs-CRP) reduction. Both interventions showed no changes in terms of safety parameters (liver and kidney function test) and no adverse reactions were found among obese participants with T2DM at 12-weeks. In conclusion, the MRT group have achieved a reduction of weight loss nearly 5% and HbA1c > 1% at 12 weeks. MRT group had greater weight loss, BMI and percentage of body fat than the SDT group at 12 weeks. The differences between groups on HbA1c were not significant. However, the observations were became significant, with a large magnitude of changes when minimising the confounder effect after excluding participants who changed type of OAD. Within the MRT group, improvements in glycemic control and CVD risks were evident, and were not observed within the SDT group. The MRT group had high adherence rate at 12 weeks. Both interventions were safe for obese participants with T2DM at 12 weeks. Further longer-term study is warranted.
Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia Sebagai memenuhi keperluan untuk ijazah Master Sains

KESAN TERAPI PENGGANTIAN MAKANAN KE ATAS BERAT BADAN, KAWALAN GLISEMIK DAN RISIKO PENYAKIT KARDIOVASKULAR DALAM KALANGAN PESAKIT OBES YANG MENGHIDAP DIABETES MELLITUS JENIS 2

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Obesiti merupakan perkara biasa dalam kalangan pesakit diabetes mellitus jenis 2 (T2DM). Menurunkan berat badan serendah 5% boleh membantu dalam memperbaiki komplikasi berkaitan dengan T2DM. Walaupun penggunaan terapi penggantian makanan (MRT) sebagai sebahagian daripada terapi pemakanan perubatan (MNT) disarankan, keberkesanannya masih belum jelas, terutamanya dalam konteks rakyat Malaysia. Kajian ini merentukan kesan MRT ke atas berat badan, kawalan glisemik dan risiko penyakit kardiovaskular (CVD) dalam kalangan pesakit obes yang menghidap T2DM. Seramai tiga puluh dua (n = 32) orang pesakit obes yang menghidap T2DM (min; umur = 46.4 ± 8.2 tahun; wanita = 34.4%; index jisim tubuh (BMI) = 31.8 ± 4.9 kg/m2; glycated hemoglobin (HbA1c) = 8.8 ± 1.5%) direkrut dari Institut Diabetes Negara, Pusat Sumber Diabetes. Peserta dikumpulkan secara rawak iaitu dalam kumpulan MRT (n = 16) atau kumpulan terapi pemakanan piawai (SDT) (n = 16) untuk kajian selama 12 minggu. Semua peserta telah menerima MNT daripada dietitian di Pusat Sumber Diabetes dengan preskripsi iso-kalori pada kadar 1200 kcal/sehari bergantung kepada keperluan peserta. Peserta dalam kumpulan MRT diminta untuk mengganti dua kali makanan mereka dengan dua set makanan pengganti dalam sehari, serta satu snek dan pelan makanan sihat untuk makan malam. Peserta kumpulan SDT pula diminta untuk mengambil tiga pelan makanan yang berasaskan karbohidrat-dikawal dan satu snek. Parameter berat badan, komposisi badan, kawalan glisemik dan risiko CVD dinilai pada garis dasar, 6 dan 12 minggu yang telah ditetapkan. Semua data yang dilaporkan adalah berdasarkan analisis intention-to-treat. Sejumlah 27 peserta menyempurnakan kajian dengan kadar penyertaan sebanyak 84.4% (MRT = 14, 87.5%; SDT = 13, 81.3%). Ciri-ciri garis dasar adalah setara antara dua kumpulan. Pada minggu ke-12, kumpulan MRT mempunyai magnitud perubahan yang besar dan signifikan (np² = 0.272, p = 0.010) serta penurunan berat badan yang ketara (83.3 ± 13.0 kg, Δ garis dasar = -3.5 ± 0.5 kg) berbanding dengan kumpulan SDT (87.2 ± 20.8 kg, Δ garis dasar = -3.5 ± 0.5 kg)
dasar = -1.1 ± 2.4 kg; P < 0.01). Peratusan penurunan berat badan dalam kumpulan MRT (Δ garis dasar = -4.1 ± 2.1%) adalah signifikan dan lebih ketara berbanding dengan kumpulan SDT (Δ garis dasar = -1.4 ± 2.5%; p < 0.01). Penurunan BMI dan peratusan lemak badan juga signifikan dalam kumpulan MRT berbanding dengan kumpulan SDT (p < 0.01). Secara umumnya, perbezaan HbA1c di antara dua kumpulan adalah tidak ketara. Menariknya, analisis meminimumkan kesan faktor luaran (confounders) dengan mengeluarkan peserta yang telah menukar ubat oral anti-diabetes (OAD) menunjukkan perbezaan ketara dengan kadar perubahan magnitud yang besar (ηp² = 0.255, p = 0.006). Kumpulan MRT mengalami kadar penurunan HbA1c dan dos OAD yang lebih besar berbanding dengan kumpulan SDT. HbA1c dalam kumpulan MRT berkurang daripada 9.1 ± 1.5% kepada 7.9 ± 1.3% (Δ garis dasar = -1.1%; p < 0.01), yang tidak dikesan dalam kumpulan SDT (garis dasar = 8.5 ± 1.5%; 12-minggu = 8.0 ± 1.1%; Δ garis dasar = -0.5%; p = 0.11). Paras glukos plasma ketika berpuasa (FPG) juga berkurang dalam kumpulan MRT (Δ garis dasar = -1.2 ± 2.2 mmol/L; p < 0.05), tetapi tidak berlaku dalam kumpulan SDT, tanpa sebarang perbezaan ketara antara dua kumpulan ini. Penurunan berat badan adalah dikaitkan dengan penurunan HbA1c. Risiko CVD cenderung untuk berkurangan dalam kumpulan MRT berbanding dengan kumpulan SDT, tetapi tiada sebarang perbezaan ditemui antara dua kumpulan ini. Kira-kira 72.5% peserta daripada kumpulan MRT patuh kepada intervensi yang dikenakan. Pematuhan terhadap MRT berkait rapat dengan pengurangan berat badan, pengurangan lemak viseral, penurunan HbA1c dan penurunan C-reaktif protein bersensitiviti-tinggi (hs-CRP). Kedua-dua intervensi ini tidak menunjukkan sebarang kesan kepada parameter keselamatan (ujian fungsi hati dan buah pinggang) dan tiada kesan sampingan yang dites dalam kumpulan peserta obes yang menghidap T2DM sepanjang 12 minggu. Kesimpulannya, kumpulan MRT mencapai penurunan berat badan hampir 5% and HbA1c >1% pada minggu ke-12. Kumpulan MRT merekodkan penurunan berat badan, BMI dan peratusan lemak badan yang lebih baik berbanding dengan kumpulan SDT. Perbezaan antara kumpulan ini dalam aspek HbA1c adalah tidak ketara. Kesan perubahan magnitud yang besar dapat dilihat dengan meminimumkan kesan faktor luaran dengan mengeluarkan peserta yang telah menukar jenis OAD. Dalam kumpulan MRT, penurunan dalam kawalan glisemik dan risiko CVD adalah jelas, yang tidak dapat dikesan dalam kumpulan SDT. Kumpulan MRT mempunyai tahap kepatuhan yang tinggi pada tempoh 12 minggu. Intervensi adalah selamat untuk peserta obes yang menghidap T2DM pada tempoh 12 minggu. Kajian lanjutan dengan tempoh masa yang lebih lama adalah diperlukan.
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I certify that a Thesis Examination Committee has met on 28 March 2018 to conduct the final examination of Gw Soon Peng on his thesis entitled "Effects of Meal Replacement Therapy on Body Weight, Glycemic Control and Cardiovascular Disease Risks in Obese Type 2 Diabetes Patients" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science.

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<tr>
<td>ADA</td>
<td>American Diabetes Association</td>
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<tr>
<td>AFES</td>
<td>ASEAN Federation of Endocrine Societies</td>
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<tr>
<td>AGI</td>
<td>Alpha-glucosidase inhibitors</td>
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<td>ANOVA</td>
<td>Analysis of variance</td>
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<td>ALP</td>
<td>Alkaline phosphatase</td>
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<td>ALT</td>
<td>Alanine aminotransferase</td>
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<tr>
<td>AST</td>
<td>Aspartate aminotransferase</td>
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<tr>
<td>BF</td>
<td>Body fat</td>
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<tr>
<td>BIA</td>
<td>Bioelectrical Impedance Analyser</td>
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<tr>
<td>BMI</td>
<td>Body mass index</td>
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<tr>
<td>BMR</td>
<td>Basal metabolic rate</td>
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<tr>
<td>CDA</td>
<td>Canadian Diabetes Association</td>
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<tr>
<td>CHD</td>
<td>Coronary heart disease</td>
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<tr>
<td>CKD-EPI</td>
<td>Chronic Kidney Disease Epidemiology Collaboration</td>
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<tr>
<td>CONSORT</td>
<td>Consolidated Standards of Reporting Trials</td>
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<tr>
<td>CPG</td>
<td>Clinical Practice Guidelines</td>
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<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
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<tr>
<td>DBP</td>
<td>Diastolic blood pressure</td>
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<tr>
<td>DPP-4</td>
<td>Dipeptidyl peptidase-4</td>
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<tr>
<td>DHA</td>
<td>Docosahexaenoic acid</td>
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<tr>
<td>DiabCare</td>
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<tr>
<td>DM</td>
<td>Diabetes Mellitus</td>
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<tr>
<td>EASD</td>
<td>European Association for the Study of Diabetes</td>
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<tr>
<td>EDTA</td>
<td>Ethylenediaminetetraacetic acid</td>
<td></td>
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<tr>
<td>eGFR</td>
<td>Estimated glomerular filtration rate</td>
<td></td>
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<tr>
<td>EI</td>
<td>Energy intake</td>
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<tr>
<td>EPA</td>
<td>Eicosapentaenoic acid</td>
<td></td>
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<tr>
<td>FPG</td>
<td>Fasting plasma glucose</td>
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<tr>
<td>GGT</td>
<td>Gamma-glutamyl transferase</td>
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<tr>
<td>GLP-1 RA</td>
<td>Glucagon-like peptide-1 receptor agonist</td>
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<tr>
<td>GTSN</td>
<td>Glycemia-targeted specialised nutrition</td>
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<tr>
<td>HbA1c</td>
<td>Glycated haemoglobin A1c</td>
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<tr>
<td>HDL-C</td>
<td>High-density lipoprotein cholesterol</td>
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<tr>
<td>HIV+</td>
<td>Human immunodeficiency virus positive</td>
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<tr>
<td>HOMA-IR</td>
<td>Homeostatic model assessment-insulin resistance</td>
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<tr>
<td>hs-CRP</td>
<td>High-sensitivity C-reactive protein</td>
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<tr>
<td>IDF</td>
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<tr>
<td>IDF-WPR</td>
<td>International Diabetes Federation-Western Pacific Region</td>
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<tr>
<td>IPAQ-SF</td>
<td>International Physical Activity Questionnaire-short format</td>
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<tr>
<td>ITT</td>
<td>Intention-to-treat</td>
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<tr>
<td>JDS</td>
<td>Japan Diabetes Society</td>
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<tr>
<td>LCD</td>
<td>Low-calorie diet</td>
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<tr>
<td>LDL-C</td>
<td>Low-density lipoprotein cholesterol</td>
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<tr>
<td>Look AHEAD</td>
<td>Look Action for Health in Diabetes</td>
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<tr>
<td>MCOM</td>
<td>Malaysian Council for Obesity Prevention</td>
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<tr>
<td>MDA</td>
<td>Malaysian Dietitians’ Association</td>
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<tr>
<td>MEMS</td>
<td>Malaysian Endocrine and Metabolic Society</td>
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<tr>
<td>MET</td>
<td>Metabolic Equivalent of Task</td>
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<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>MNT</td>
<td>Medical nutrition therapy</td>
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<tr>
<td>MOH</td>
<td>Ministry of health</td>
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<tr>
<td>MRT</td>
<td>Meal replacement therapy</td>
<td></td>
</tr>
<tr>
<td>MUFA</td>
<td>Monounsaturated fatty acids</td>
<td></td>
</tr>
<tr>
<td>N/A</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td>NADI</td>
<td>National Diabetes Institute / Institut Diabetes Negara</td>
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<tr>
<td>NCP</td>
<td>Nutrition Care Process</td>
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<tr>
<td>NGO</td>
<td>Non-governmental organisation</td>
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<tr>
<td>NHMS</td>
<td>National Health and Morbidity Survey</td>
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<tr>
<td>OAD</td>
<td>Oral Anti-Diabetes Drugs</td>
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<tr>
<td>PAL</td>
<td>Physical activity level</td>
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<tr>
<td>PATH</td>
<td>Patient Algorithm Therapy for Metabolic Control</td>
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<tr>
<td>PEG</td>
<td>Polyethene glycol</td>
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<tr>
<td>PES</td>
<td>Problems, Etiology, Signs and Symptoms</td>
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<td>PDM</td>
<td>Malaysian Diabetes Association</td>
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<tr>
<td>PUFA</td>
<td>Polyunsaturated fatty acids</td>
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<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
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<tr>
<td>SBP</td>
<td>Systolic blood pressure</td>
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<tr>
<td>SD</td>
<td>Standard deviation</td>
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<td>SDT</td>
<td>Standard dietetic therapy</td>
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<tr>
<td>SGLT-2</td>
<td>Sodium glucose cotransporter-2</td>
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<tr>
<td>SPSS</td>
<td>Statistical Package for Social Science</td>
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<tr>
<td>SST</td>
<td>Serum separator tube</td>
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<tr>
<td>T2DM</td>
<td>Type 2 Diabetes Mellitus</td>
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<tr>
<td>TC</td>
<td>Total cholesterol</td>
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<tr>
<td>TC/HDL-C</td>
<td>Total cholesterol/high-density lipoprotein cholesterol ratio</td>
<td></td>
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<tr>
<td>tDNA</td>
<td>Transcultural Diabetes Nutrition Algorithm</td>
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<tr>
<td>TG</td>
<td>Triglycerides</td>
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<tr>
<td>TZD</td>
<td>Thiazolidinediones</td>
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<tr>
<td>U.K.</td>
<td>United Kingdom</td>
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<tr>
<td>U.S.</td>
<td>United States</td>
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<tr>
<td>UKPDS</td>
<td>United Kingdom Prospective Diabetes Study</td>
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<tr>
<td>USA</td>
<td>United States of America</td>
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<tr>
<td>USD</td>
<td>United States Dollar</td>
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<tr>
<td>VF</td>
<td>Visceral fat</td>
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<tr>
<td>WC</td>
<td>Waist circumference</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<tr>
<td>β</td>
<td>Beta</td>
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<tr>
<td>η²</td>
<td>Partial eta-squared</td>
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<td>Δ</td>
<td>Changes</td>
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<td>ω</td>
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CHAPTER 1

INTRODUCTION

1.1 Background of Study

The prevalence of Type 2 Diabetes Mellitus (T2DM) in Malaysia is increasing dramatically. In 2015, the prevalence of diabetes among Malaysian population age ≥ 18 years old stood more than 17% as compared to 2006 which was about 12% (Institute of Public Health, 2015; Wan Nazaimoon et al., 2013). About 75% of people with diabetes in Malaysia were not achieving optimal glycemic control (Barakatun-Nisak et al., 2013; Mafauzy et al., 2011).

Obesity is common in diabetes with almost 65 – 80% are overweight and obese at diagnosis (Pal et al., 2015). In 2012, National Diabetes Registry Malaysia conducted a study reported that about 83% of patients with T2DM were either overweight or obese, a substantial rise from nearly 67% in 2003 (Ministry of Health: Malaysia, 2015; Mafauzy et al., 2011).

In obese patients with T2DM, a weight loss by 5 - 10% of the initial weight has been associated with an improvement in diabetes-related outcomes (Wing et al., 2011; Schwartz and Kohl, 2010; Anderson et al., 2003). The changes associated with weight loss was achieved clinically meaningful outcomes of HbA1c reduction by 0.5% - 1.1% and CVD risks improvement (Wing et al., 2011; Van Gaal et al., 2005). Optimal glycemic control had reduced the long-term T2DM complications (Schwartz, 2013).

The management of obesity with diabetes include medical nutrition therapy (MNT), pharmacological intervention and bariatric surgery (American Diabetes Association, 2016; Ministry of Health: Malaysia, 2015). MNT plays a significant role in achieving weight loss, glycemic control and CVD risks. MNT through dietary therapy, physical activity and behaviour therapy is capable of producing optimum glycemic outcomes for obese adults with T2DM (Evert et al., 2013).

Dietary therapy is defined as the provision of a low-calorie diet (LCD), a diet with ~1200 kcal/day is commonly used for obesity management. (Ministry of Health: Malaysia, 2004; Saris, 2001). In general, LCD is implemented through self-restriction strategy (American Diabetes Association et al., 2008). Using self-restricted LCD could improve HbA1c by 0.5% - 1% in 6 months (Barakatun-Nisak et al., 2013; Dworatzek et al., 2013). However, it is a daunting task and would lead to poor adherence with only 16.4% who adhered to LCD (Tan et al., 2011a). While LCD is a safe with lesser side effects, poor adherence could be related to a difficulty to control food intake (Siti Maisharah et al., 2011; Rossner and Flaten, 1997).
Meal replacement therapy (MRT) is the integral component of the management of T2DM especially for weight loss and weight maintenance which has been recommended by American Diabetes Association (2013) and Malaysian Dietitians’ Association (MDA) (2013). An MRT is designed to be a component of LCD which can replace one or two meals per day. At the same time, a healthy solid meal and snacks would be incorporated to make up the balance of the recommended daily energy intake (Dworatzek et al., 2013).

Weight loss with MRT was able to reduce 5 - 10% weight, which associated with clinically meaningful improvement in glycemic control and CVD risks (Brown et al., 2015, Dworatzek et al., 2013; Craig, 2013). The Look Action for Health in Diabetes (Look AHEAD) Research Group (2014) conducted weight losses study for 8 years by using an intensive lifestyle intervention incorporating with MRT study among overweight and obese adults with T2DM. This intensive research has successfully produced clinically meaningful weight loss (≥ 5% of their initial weight) in 50% of patients with T2DM. Hence, MRT should be emphasised given the poor glycemic control among obese patients with T2DM in Malaysia. Also, when compared with a standard dietetic therapy (SDT) that commonly included in self-restricted LCD approaches, MRT serves as a tool to aid dietary adherence and perceived to be convenient (Brown et al., 2015).

1.2 Statement of Research Problem

Many types of research have reported that higher body mass index (BMI) relatively increase the severity of T2DM and its complications (Schienkiewitz et al., 2006; Pi-Sunyer, 2002). There is also a parallel increase in obesity rate among individuals with T2DM (Ghee, 2016), hence suggesting critical needs to establish an effective weight loss protocol for obese with T2DM.

The role of a dietitian is essential in diabetes management. Current practices support the used of LCD based-on restriction of the food to achieve weight loss among obese adults with T2DM. However, the adherence on LCD of food-based is a challenge and difficult to measure. The incorporation of MRT into LCD prescriptions may be used to support better adherence to produce better weight loss and health outcomes including glycemic control and CVD risk (Craig, 2013, World Health Organization, 2003c). Study has shown that the MRT may be a simple tool to assist achievement in LCD results (Look AHEAD Research Group, 2014). Its simplicity could enhance adherence and ensure weight loss. This is because it is believed that the MRT can be used to educate obese patients with T2DM to kick-start robust initial weight loss results (Look AHEAD Research Group, 2014). Achieving initial weight loss has a strong association with the overall success of weight loss treatment, even as little as 1 kg weight loss (Elfhag and Rossner, 2010). Indeed, the more weight loss happened at the initial stage, the more weight loss will be produced subsequently (Elfhag and Rossner, 2010).
MRTs as part of weight loss program in T2DM are recommended by the transcultural Diabetes Nutrition Algorithm (tDNA), Malaysian Dietitian’s Association (2013) (MDA) and clinical practice guidelines (CPG) on management of T2DM (Ministry of Health: Malaysia, 2015). However, the references used to substantiate tDNA and MDA were primarily based on caucasian studies (Look AHEAD Research Group, 2014; Franz et al., 2010). Besides, the standardized MRT research-based tools for weight loss is still at its infancy in Malaysia. Thus, there is a need to identify the effective translation of MRT research in a real-life community where T2DM individuals are usually exposed to various challenges to enhance self-management practices including dietary choices (Gibson and Sainsbury, 2017; Lindberg et al., 2013; Sharma and Padwal, 2010; Mitri and Hamdy, 2009; Ribisl et al., 2007; Grave et al., 2005).

The effectiveness of MRT among obese individuals with T2DM in Malaysia was only published recently (Chee et al., 2017). This study tested the effectiveness of MRT among 115 of obese adults with T2DM based-on sub-urban area setting in Seremban, Negeri Sembilan. In this study, the MRT is provided free of charge throughout the study and majority of the participants were Malays. They found that the used of MRT together with behavioral changes were effective to reduce HbA1c by -1.1% and sustained it for 6 months after the intervention had stopped (Chee et al., 2017). While the study is longer and the sample size is larger than the current study, the current study added substantial information for the application of MRT based-on urban area setting and extension to other ethnic groups including Indian and Chinese community. Current study is crucial due to urban residents and Indian ethnicity in Malaysia comprised of the highest prevalence of T2DM (Tee and Yap, 2017) and the Chinese ethnicity prevalence of T2DM is getting higher since 2006 (Hussein et al., 2015). The application of MRT with urban setting and non-Malay patients would certainly fill in the gap of Malaysia data.

As in Chee et al. (2017) study and other studies in the world (Look AHEAD Research Group, 2014; Shirai et al., 2013; Keogh and Clifton, 2012; Sun et al., 2008; Li et al., 2005; Yip et al., 2001), the MRT was given free of charge that may limit the generalization of the study outcomes in a real-life setting where the resources from the government are limited (Thomas et al., 2011). This study provided a partial support rather than total support for the MRT to ensure that the individuals may benefits from their self-effort and sustained it for a longer period of time. Therefore, this study seeks to evaluate the effect of MRT to induce minimum 5% weight loss on initial body weight and to reduce 0.5% of the HbA1c level in obese adults with T2DM on 12 weeks intervention, with adequately statistical powered.

1.3 Study Significance

The current study provides evidence for the important on the use of MRT as an effective weight loss tool to achieve 5 – 10% weight reduction from baseline body weight in 12 weeks among obese individuals with T2DM. Initial weight loss is important to ensure long-term weight loss achievement.
This study adds to the literature on adherence to MRT as a dietary therapy, improving one of the most challenging aspects of diabetes care. Furthermore, findings from this study can potentially be used as a reference to managing obesity, glycemic control and CVD risks through Look AHEAD research adoption and dissemination, translating from the study in the United States to Asian countries like Malaysia. This development and intervention evaluation are necessary especially to improve diabetes outcome at the community level in patients with T2DM who are obese.

From a clinical practice standpoint, this study is relevant and timely needed. Since MRT is recommended in the MNT guidelines, this study would clarify the algorithm specificity and effectiveness of MRT on weight loss and clinical meaningful among obese adults with T2DM in Malaysia. In this study, the algorithm of MNT had incorporated to the application of nutrition care process (NCP) on the management of weight loss among obese patients with T2DM. Eventually, this synergistics combination of MNT and NCP would be developed to effectively assist body weight reduction of patients. Besides, the meal replacement was partially self-paid by participants who were randomized into MRT intervention. This could exemplified the “real-world” clinical setting. The participants make an effort to purchase the products of meal replacement could contributed to higher appreciation and hence increased the adherence rate of MRT.

Nonetheless, this study recommendation for weight loss via MRT as part of weight loss program should be encouraged to all obesity-related patients including adults with diabetes who are aiming to achieve greater weight loss, especially at the initial stage.

1.4 Research Questions

What is the effects of MRT compared to SDT on body weight, glycemic control and CVD risks among obese patients with T2DM at 12 weeks?

1.5 Study Objectives
1.5.1 General Objectives

To investigate the effects of meal replacement therapy (MRT) on body weight, glycemic control and cardiovascular disease (CVD) risks among obese patients with T2DM.
1.5.2 Specific Objectives

1. To determine and compare the effect of MRT versus standard dietetic therapy (SDT) on body weight and body composition (percentage of body fat and visceral fat) among obese patients with T2DM at 12 weeks.
2. To determine and compare the effect of MRT versus SDT on glycemic control (HbA1c and fasting plasma glucose) and CVD risks (blood pressure, lipid profile – LDL-C, TG, HDL-C, TC and TC/HDL-C, and inflammatory marker – hs-CRP) among obese patients with T2DM at 12 weeks.
3. To determine the participants’ MRT adherence at 12 weeks.
4. To assess the participants’ safety parameters (liver function tests – GGT, ALT, ALP, AST, total bilirubin and albumin, and kidney function tests – creatinine, eGFR and urea) at 12 weeks.

1.6 Hypothesis

The study hypothesised that:
1. MRT would be reduced body weight and body composition significantly as compared to SDT among obese patients with T2DM at the 12 weeks of study.
2. MRT would be improved glycemic control and CVD risks significantly as compared to SDT among obese patients with T2DM at the 12 weeks of study.
3. MRT group would be achieved high adherence at the 12 weeks of study.
4. MRT and SDT groups remain unchanged on liver and kidney function tests at the 12 weeks of study.

1.7 Conceptual Framework

The conceptual framework of this study is visualised in Figure 1.1. The MRT in this context was designed as partial meal replacement for main meal to achieve a healthy LCD among obese adults with T2DM. The diet modification for MRT comprised of two meal replacements (breakfast and lunch), a snack and a healthy meal plan (food-based) for dinner.
Figure 1.1: Conceptual Framework

The primary outcomes following the MRT were body weight and body composition. The effect of MRT on glycemic control and CVD risks are identified as the secondary outcomes. These secondary outcomes were either affected directly by MRT or due to body weight changes as a consequence of MRT effect.

Although the principle of good glycemic control should be prioritised in every T2DM patient, the effectiveness of reducing body weight and body composition are equally essential for obese patients with T2DM (American Diabetes Association et al., 2008). Obesity is known to induce insulin resistant that leads to hyperglycemia and exacerbates the metabolic abnormalities of T2DM, in particular, glycemic control and CVD risks (Horton et al., 2010). On the other hand, weight loss among obese adults with T2DM is constantly proven to deliver effective clinical improvement and plays an important long-term role in improving glycemic control (Wing et al., 2011; Look AHEAD Research Group and Wing et al., 2010).

A clinically significant weight loss is ≥ 5% body weight reduction from initial body weight among obese adults with T2DM. The ≥ 5% of weight loss would accompany with the reduction in HbA1c levels by 0.6 - 1.0% and improvement of CVD risk factors including parameters of blood pressure, LDL-C, TG, HDL-C and hs-CRP. In few studies, these improvement led to reduction in medications for diabetes, hypertension and lipid (Wing et al., 2011; Klein et al., 2004; Ziccardi et al., 2002; National Heart, Lung, and Blood Institute, 1998).
The challenges included goal setting, pharmacotherapy, body metabolic and lifestyle have been identified in the previous studies to confound the improvement in primary and secondary outcomes (Gibson and Sainsbury, 2017; Lindberg et al., 2013; Sharma and Padwal, 2010; Mitri and Hamdy, 2009; Ribisl et al., 2007; Grave et al., 2005). In this study, the challenges of goal setting were consistently highlighted during the intervention to improve the outcomes. Pharmacotherapy, body metabolic and lifestyle challenges have been identified and considered to minimise their confounding effect on the good outcomes in this study.
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