Relationship between Obesity-related Hormone Peptides and Quality of Life in Obese Women among Different Traditional Chinese Medicine Syndrome Groups

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Abstract

The aim of this study was to explore the relationship between obesity-related hormone peptides and quality of life in obese women among different traditional Chinese medicine (TCM) syndrome groups (證型 zhèng xíng). 260 obese women met with age between 20 and 65 years old and body mass index (BMI) $\geq$ 27 kg/m^2, were recruited. The participants filled out a questionnaire on obese TCM syndrome groups, which was designed by professional TCM doctors, and two questionnaires on quality of life (QOL), WHOQOL-BREF Taiwan version and MOS Short Form-12 (SF-12). Data of biochemical characteristics and obesity-related hormone peptides were collected at the same time. According to the responses provided, the obese subjects were classified into spleen deficiency with dampness encumbrance syndrome (脾虛濕阻證 pí xū shī zǔ zhèng; SDD), stomach heat with dampness encumbrance syndrome (胃熱濕阻證 wèi rè shī zǔ zhèng; SHD), liver depression and qi stagnation syndrome (肝鬱氣滯證 gān yù qì zhì zhèng; LDQ), dual spleen-kidney deficiency syndrome (脾腎兩虛證 pí shèn liǎng xū zhèng; SKD), yin deficiency with internal heat syndrome (陰虛內熱證 yīn xū nèi rè zhèng; YDI) and a control group. For physical conditions, SDD group had significantly higher means in weight and BMI compared with the control group. The insulin and leptin levels in SHD group were significantly higher than those in the control group. The LDQ group showed marked decrease in mental condition scores compared with the control group. This study found that obese women in the SDD group were fatter than those in the control group. SHD group might have greater influence on the regulation of obesity-related hormone peptides. The LDQ group had poor QOL than the control group. Analysis of TCM syndrome groups among obese women merits further investigation.

Key words: Traditional Chinese medicine syndrome groups, Obesity, Quality of life, Oesity-related hormone peptides

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Introduction

Obesity is becoming a global epidemic and an important health problem. Its prevalence has trebled since the 1980s, especially in developed countries. Many studies have shown association between obesity and other health problems including cardiovascular diseases, type-2 diabetes, sleep apnea, obesity-related cancers, osteoarthritis, and depression (Must et al., 1999; Mokdad et al., 2003; Dixon, 2010).

Previous research also showed that our appetite and energy homeostasis were regulated by different obesity-related hormone peptides, such as leptin, ghrelin, peptide YY3–36, adiponectin, resistin, and insulin (Flier and Maratos, 1998; Gale et al., 2004). In addition, there was also significant relationship between levels of obesity-related hormone peptides and QOL (Peyrot et al., 2011). Obesity not only influences a person's physiological conditions but also has a substantial negative impact on his/her QOL (Fine et al., 1999; Fontaine and Barofsky, 2001; Marchesini et al., 2003).

According to TCM theories, obese patients can be classified into different syndrome groups (證型 zhèng xíng) on the basis of their symptoms and according to the physician's clinical experiences. Nevertheless, there is yet no standard approach to such classification. Hence, there is a need to develop a self-reported questionnaire on symptoms to facilitate the classification of obese TCM syndrome groups. In addition, understanding the relationship between obesity-related hormone peptides and QOL in different obese TCM syndrome groups can help TCM health workers provide better care to the patients. In view of the above, we conducted this cross-sectional study to explore the relationship between obesity-related hormone peptides and QOL in different obese TCM syndrome groups.

Method

Study design and participants

This was a cross-sectional study conducted from January 2010 to December 2010 in Branch of Linsen and Chinese Medicine, Taipei City Hospital, Taiwan. Of 572 obese women prescreened at our outpatient clinic, a total of 260 were enrolled. The inclusion criteria and exclusion criteria are shown in Table 1. The protocol was approved by the Human Ethics Committee of Taipei City hospital.

Obese TCM syndrome groups and control group

The enrolled subjects were examined by TCM

Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria
1. Female
2. Age between 20 and 65 years old
3. Body mass index $\geq$ 27 kg/m^2
4. Willing to participate in and fill out the questionnaires for this trial

Exclusion Criteria
1. Endocrine diseases, e.g., thyroid disorder, pituitary disorder, and sex gland disorder
2. Heart diseases, e.g., arrhythmia, heart failure, and myocardial infarction, as well as patients with pacemaker
3. Allergy and immunologic diseases
4. High aminotransferases (alanine, aspartate > 80 IU/L) or high serum creatinine (> 2.5 mg/dL)
5. Pregnant or lactating or childbirth within 6 months
6. Stroke or otherwise unable to exercise
7. Management for weight control within 2 months
8. Any other conditions deemed unsuitable for trial as evaluated by physician-in-charge

practitioners and diagnoses were made on the basis of the examination, symptoms reported by the patients and the practitioner's experience. According to TCM concepts, our clinical experiences and related studies, five most common TCM syndrome groups of obese patients were defined (WHO, 2007; Zhu et al., 2010). These groups are respectively characterized by spleen deficiency with dampness encumbrance syndrome (脾虛濕阻證 pí xū shī zǔ zhèng; SDD), stomach heat with dampness encumbrance syndrome (胃熱濕阻證 wèi rè shī zǔ zhèng; SHD), liver depression and qi stagnation syndrome (肝鬱氣滯證 gān yù qì zhì zhèng; LDQ), dual spleen-kidney deficiency syndrome (脾腎兩虛證 pí shèn liǎng xū zhèng; SKD) and yin deficiency with internal heat syndrome (陰虛內熱證 yīn xū nèi rè zhèng; YDI). To our knowledge, there are no existing questionnaires or diagnostic tools for classifying obese patients. Hence, according to TCM concepts, we developed a self-reported questionnaire on patient symptoms as a diagnostic tool. Ten TCM doctors with clinical experience met and came up with four yes-no questions under each syndrome group for diagnosing obese patients. The questionnaire designed is shown in Table 2.

Obese patients with more than two symptoms reported for each syndrome in the questionnaire would be classified into that particular syndrome group. For patients with the same number of symptoms reported for more than one syndrome group, the classification would be made by the physician according to other information such as pulse and tongue appearance.

The control group comprised patients not classified into any of the syndrome groups. Validation test results showed an alpha coefficient of 0.86 and Cronbach's

Table 2. Questionnaire on traditional Chinese medicine syndrome groups

In the past week, did you often have the following symptoms? (Often means more than 8 hours per day and more than four days per week)		
a. Spleen deficiency with dampness encumbrance syndrome (脾 虛 濕阻證 pí xū shī zǔ zhèng; SDD)		
(1) Leg pitting edema	Yes	No
(2) Shortness of breath	Yes	No
(3) Anorexia	Yes	No
(4) Abdominal distention	Yes	No
b. Stomach heat with dampness encumbrance syndrome (胃熱濕阻 證 wèi rè shī zǔ zhèng; SHD)		
(1) Swift digestion with frequent hunger	Yes	No
(2) Aphthous stomatitis	Yes	No
(3) Bitter taste in the mouth	Yes	No
(4) Polydipsia	Yes	No
c. Liver depression and qi stagnation syndrome (肝鬱氣滯證 gān yù qì zhì zhèng; LDQ)		
(1) Chest tightness	Yes	No
(2) Insomnia	Yes	No
(3) Agitation and irritability	Yes	No
(4) Bitter taste in the mouth	Yes	No
d. Dual spleen-kidney deficiency syndrome (脾腎兩虛證 pí shèn liǎng xū zhèng; SKD)		
(1) Fear of cold	Yes	No
(2) Lassitude in loin and legs	Yes	No
(3) Frequent urination	Yes	No
(4) Tinnitus and hard of hearing	Yes	No
e. Yin deficiency with internal heat syndrome (陰虛內熱證 yīn xū nèi rè zhèng; YDI)		
(1) Night sweating	Yes	No
(2) Dry throat and mouth	Yes	No
(3) Lassitude in loin and legs	Yes	No
(4) Aphthous stomatitis	Yes	No

alpha coefficient of 0.88, indicating that the questionnaire has good reliability.

Quality of life

To measure the QOL among our subjects, we used two self-administered QOL questionnaires. One was WHOQOL-BREF, Taiwan version which was well validated with consistency coefficients ranging from 0.70 to 0.77 (Yao et al., 2002). The WHOQOL-BREF questionnaire evaluated QOL in physical, psychological, social and environmental domains, with scores ranging from 0 to 100. The other self-administered QOL questionnaire we used was MOS Short Form-12 (SF-12). There are 12 items measuring eight concepts: physical functioning, role limitations due to physical health problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional health, and mental health. Responses to these questions are transformed into two scores, physical condition score 12 (PCS-12) and mental condition score (MCS-12) , to reflect physical and mental conditions, respectively. The general population has a mean of 50 and a standard deviation of 10 (Ware et al., 1996; Ware et al., 1998). Higher scores represent better health.

Analysis of obesity-related hormone peptides

The levels of obesity-related hormone peptides, including leptin, insulin, ghrelin and adiponectin, were measured in the morning after 8-9 hours of fasting. The whole blood sample was drawn and centrifuged at 4℃, with 1 ml of the sample rapidly frozen at -80℃ for the subsequent radioimmunoassay concentration analysis. Leptin was detected by the Millipore Human Leptin assay (Millipore, St. Charles, MO, USA) using I^{125}-labled human leptin antiserum with a sensitivity of 0.5 ng/ml for a 100-μl sample. Ghrelin and adiponectin were detected by Millipore Ghrelin RIA Kits (Millipore, St. Charles) and Millipore Adiponectin RIA kits (Millipore, St. Charles) with a sensitivity of 93 pg/ml and 1ng/ml, respectively. We used the same process as that for leptin detection only with different I^{125}-labled antibodies specific for ghrelin or adiponectin. BioSource INS-IRMA Kits (BioSource Europe S.A., Nivelles, Belgium) were employed to determine the level of insulin in serum as previously reported (Starr et al., 1978; Agin et al., 2006). Sampling would be reported if a difference exceeding 10% CV was found between duplicated results of the sample. Following the approach of Matthews et al., we used the homeostasis model assessment for insulin resistance (HOMA-IR) for measuring insulin resistance of our subjects (Matthews et al. 1985).

Outcomes measurement

The major outcomes included the mean QOL scores and levels of obesity-related hormone peptides in different TCM syndrome groups and the control group. The outcomes were evaluated in terms of body weight, BMI and waist circumference, biochemical characteristics of blood sample including fasting blood sugar, triglyceride, total cholesterol levels, obesity-related hormone peptides, and QOL scores on the WHOQOL-BREF and MOS Short Form-12 scores of different obese TCM syndrome groups classified by obese TCM questionnaire. All measurements were made after 8-9 hours of fasting using a standardized method, as detailed in our previous research (Hsu et al., 2008), and all participating physicians received prior training before the study on how to interview the patients and assist them in completing the questionnaires.

Statistical analysis

The data were analyzed using SPSS software (version 17.0, Chicago, IL.) One-way ANOVA tests were

Table 3.Difference in basis data between control group and different obesity traditional Chinese medicine syndrome groups

	Control	SDD[a]	SHD[b]	LDQ[c]	SKD[d]	YDI[e]	Total
Number (%)	26(10)	52(20)	45(17.3)	52(20)	51(19.6)	34(13.1)	260
Basic Data							p-value
Age, years	43.1(10.9)	38.6(11.2)	38.9(12.2)	42.0(11.1)	42.5(10.6)	40.9(11.1)	0.30
Height, cm	158.1(5.0)	160.5(4.8)	159.2(5.9)	158.7(5.2)	158.5(5.5)	160.5(4.6)	0.17
Weight, kg	74.9(12.12)	82.8(13.9)**	79.7(13.7)	74.5(9.2)	73.8(8.5)	76.00(8.5)	<0.001
Body mass index, kg/m^2	29.9(3.9)	32.1(4.94)*	31.4(4.8)	29.5(2.9)	29.5(3.2)	29.5(2.5)	0.001
Waist circumference, cm	95.6(10.4)	96.5(10.3)	98.8(10.5)	94.3(8.9)	93.6(8.2)	93.5(6.5)	0.06
Hip circumference, cm	109.5(9.2)	112.4(10.3)	110.6(9.0)	107.7(6.5)	107.4(7.3)	107.8(5.9)	0.02
Systolic blood pressure , mmHg	136.1(22.5)	132.7(15.1)	136.6(18.7)	131.4(13.7)	130.2(17.6)	130.3(15.1)	0.23
Diastolic blood pressure , mmHg	79.2(12.2)	81.6(12.4)	81.6(12.9)	79.5(10.4)	79.6(8.2)	79.12(10.2)	0.78
Heart rate, times/min	78.2(9.4)	81.4(10.9)	78.7(12.9)	76.7(9.8)	79.2(9.1)	77.2(13.6)	0.37

The data are presented with mean (SD)

a, SDD = spleen deficiency with dampness encumbrance syndrome (脾虛濕阻證 pí xū shī zǔ zhèng)   b, SHD = stomach heat with dampness encumbrance syndrome (胃熱濕阻證 wèi rè shī zǔ zhèng)   c, LDQ = liver depression and qi stagnation syndrome (肝鬱氣滯證 gān yù qì zhì zhèng)   d, SKD = dual spleen-kidney deficiency syndrome (脾腎兩虛證 pí shèn liǎng xū zhèng)   e, YDI = yin deficiency with internal heat syndrome (陰虛內熱證 yīn xū nèi rè zhèng)

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, vs. control group

employed to examine the means among obese women in different TCM syndrome groups. T-tests were employed to examine the difference in mean between the control group and other obese TCM syndrome groups. All *p* values were two-tailed and considered statistically significant at α level of 0.05.

Results

Demographics and clinical features of participants

Among the 572 obese patients screened at our outpatient clinic, a total of 260 fulfilled with our inclusion and exclusion criteria and completed both questionnaires. The mean of age, weight, BMI, and waist circumference were 41.0 ± 11.5 years, 77.2 ± 11.6 kg, 30.4 ± 4.0, 95.4 ± 9.4 cm, respectively.

Basic data

Table 3 displays difference in basic data between the control group and different obese TCM syndrome groups. As can be seen, there was significant difference in weight and BMI between the SDD group and the control group; that is, obese patients with SDD were fatter than the control group.

Biochemical characteristics and obesity-related hormone peptides

As seen in Table 4, there was no significant difference in biochemical characteristics between the control group and the obese TCM syndrome groups. As for obesity-related hormone peptides, both insulin and leptin levels

were markedly higher in the SHD group than in the control group, while the ghrelin level of the SHD, LDQ, SKD, and YDI groups were significantly lower than that of the control group. The control group had the lowest insulin and leptin levels but the highest ghrelin level.

QOL scores

As seen in Table 5, there was no difference in WHOQOL-BREF scores between the control and the obese TCM syndrome groups. With respect to SF-12 QOL scores, there was significant difference in MCS-12 score between the LDQ group and the control group, with obese patients having LDQ having the lowest MCS score.

Discussion

Classification of TCM syndrome groups is an important guide for TCM physicians when choosing the treatment of choice for their patients. However, there has been little discussion on TCM syndrome groups among obese women. In the present study, among the five TCM syndrome groups, SDD and LDQ have higher prevalence, each accounting for 20% (52/260) of our obese subjects.

In terms of basic data, no significant difference was observed between the control group and the different obese TCM syndrome groups. Only the group with SDD showed higher body weight and larger BMI than the control group. According to TCM concepts, all obese patients have abnormal body weight, but the group with SDD seemed to have worse digestive function, which

Table 4. Biochemical characteristics and obesity-related hormone peptides of control group and different obesity traditional Chinese medicine syndrome groups

	Control	SDD[a]	SHD[b]	LDQ[c]	SKD[d]	YDI[e]	Total
Number (%)	26(10)	52(20)	45(17.3)	52(20)	51(19.6)	34(13.1)	260
Biochemical Characteristics							p-value
Glucose, mg/dl	99.5(14.6)	97.8(16.2)	99.2(17.8)	97.4(26.4)	108.2(48.3)	9.3(27.1)	0.44
Hemoglobin A1c , %	6.0(0.5)	5.9(0.9)	5.8(0.5)	5.8(0.4)	5.9(0.7)	5.6(0.4)	0.50
Creatinine, mg/dl	0.7(0.1)	0.8(0.1)	0.7(0.1)	0.7(0.1)	0.8(0.2)	0.7(0.1)	0.60
Alanine aminotransferase , U/l	30.5(25.8)	40.3(32.8)	34.4(27.0)	35.5(27.1)	29.5(17.3)	38.0(42.4)	0.49
Cholesterol, mg/dl	203.0(35.7)	205.7(35.1)	203.5(37.1)	200.4(31.3)	198.3(37.5)	199.6(30.3)	0.91
Triglyceride, mg/dl	129.8(59.0)	133.4(67.9)	145.0(77.9)	136.8(67.8)	130.7(59.9)	142.2(53.5)	0.88
HDL-C[f], mg/dl	47.5(11.7)	47.0(12.0)	52.1(11.6)	52.0(13.4)	49.3(11.7)	49.2(11.3)	0.20
LDL-C[g], mg/dl	127.2(42.3)	140.0(38.7)	121.2(34.7)	123.7(26.8)	127.2(35.4)	144.5(34.7)	0.12
Obesity-Related Hormone Peptides							
Insulin, IU/ml	12.6(6.6)	13.6(8.1)	18.3(8.7)*	16.0(14.7)	14.5(10.9)	16.0(11.1)	0.23
Leptin, ng/ml	16.8(11.0)	19.3(9.2)	23.5(8.2)*	20.0(8.3)	19.1(8.9)	18.5(7.8)	0.04
Ghrelin, pg/ml	819.2(359.9)	747.6(315.9)	590.2(308.1)*	565.8(272.1)*	647.6(351.1)*	569.4(289.5)*	0.002
Adiponectin, ug/ml	20.8(6.3)	21.6(8.2)	21.2(3.3)	21.3(4.5)	20.5(5.6)	20.5(4.5)	0.89
HOMA-IR indexh	3.2(2.0)	3.3(2.5)	4.5(2.7)	3.9(3.7)	3.8(3.0)	3.8(2.6)	0.40

The data are presented with mean (SD)

a, SDD = spleen deficiency with dampness encumbrance syndrome (脾虛濕阻證 pí xū shī zǔ zhèng) b, SHD = stomach heat with dampness encumbrance syndrome (胃熱濕阻證 wèi rè shī zǔ zhèng) c, LDQ = liver depression and qi stagnation syndrome (肝鬱氣滯證 gān yù qì zhì zhèng) d, SKD = dual spleen-kidney deficiency syndrome (脾腎兩虛證 pí shèn liǎng xū zhèng) e, YDI = yin deficiency with internal heat syndrome (陰虛內熱證 yīn xū nèi rè zhèng) f, HDL-C = high density lipoprotein cholesterol
g, LDL-C = low density lipoprotein cholesterol h, HOMA-IR = homeostasis model assessment for insulin resistance
*p < 0.05, **p < 0.01, ***p < 0.001, vs. control group*p < 0.05, **p < 0.01, ***p < 0.001, vs. control group

Table 5.Quality of life scores of control group and different obesity traditional Chinese medicine syndrome groups

	Control	SDD[a]	SHD[b]	LDQ[c]	SKD[d]	YDI[e]	Total
Number (%)	26(10)	52(20)	45(17.3)	52(20)	51(19.6)	34(13.1)	260
SF-12 QOL Scores							p-value
PCS-12[f]	47.3(7.7)	44.7(7.4)	46.5(8.8)	47.0(7.1)	44.3(8.5)	47.1(7.1)	0.29
MCS-12[g]	48.5(11.6)	44.3(8.1)	45.0(8.5)	43.3(10.5)*	44.1(10.0)	49.0(7.1)	0.04
WHOQOL-BREF Scores							
Physical	66.0(21.4)	62.1(12.3)	64.8(17.1)	65.4(13.1)	63.3(15.1)	70.6(10.7)	0.18
Psychological	75.3(18.9)	72.1(15.6)	72.1(11.8)	69.6(14.2)	71.6(17.7)	79.3(9.9)	0.08
Social	75.6(14.4)	71.9(12.2)	74.0(10.8)	73.0(10.2)	74.8(15.8)	78.7(11.0)	0.41
Environmental	76.0(15.8)	71.7(12.6)	73.6(12.1)	73.0(11.9)	73.9(15.8)	79.9(6.0)	0.08

The data are presented with mean (SD)

a, SDD = spleen deficiency with dampness encumbrance syndrome (脾虛濕阻證 pí xū shī zǔ zhèng) b, SHD = stomach heat with dampness encumbrance syndrome (胃熱濕阻證 wèi rè shī zǔ zhèng) c, LDQ = liver depression and qi stagnation syndrome (肝鬱氣滯證 gān yù qì zhì zhèng) d, SKD = dual spleen-kidney deficiency syndrome (脾腎兩虛證 pí shèn liǎng xū zhèng) e, YDI = yin deficiency with internal heat syndrome (陰虛內熱證 yīn xū nèi rè zhèng) f, PCS = physical condition score g, MCS = mental condition score
*p < 0.05, **p < 0.01, ***p < 0.001, vs. control group

might account for the higher body weight and larger BMI than the control group.

As seen in Table 4, there were statistically significant differences in insulin, leptin and ghrelin levels between the control group and the different obese TCM syndrome groups. Many obesity-related hormone peptides might regulate our appetite and energy homeostasis. Ghrelin, which is a hormone produced mainly by P/D1 cells lining the fundus of the human stomach and epsilon cells of the pancreas that stimulates hunger (Inui et al. 2004). It is considered the counterpart of leptin, produced by adipose tissue, which induces satiation when present at higher levels. Obese patients tend to have decreased ghrelin levels but increased leptin levels, and the effects of ghrelin on energy homeostasis are opposite to those of leptin (Cummings et al., 2002; Zigman and Elmquist, 2003). In this study, we found the ghrelin level in obese

patients with SHD, LDQ, SKD and YDI lower than that in the control group. In addition, obese patients with SHD had higher insulin and leptin level compared with the control group. Hence, we consider that SHD in obese patients might have greater influence on the regulation of obesity-related hormone peptides.

In addition to influencing our pathological conditions, obesity has profound adverse physical, social, economic consequences and environment that can negatively affect QOL (Marchesini et al., 2003; Jia and Lubetkin, 2005; Wee et al., 2008). To our knowledge, there was no study comparing QOL among different obese TCM syndrome groups. As seen in Table 5, there were statistically significant in trend with poor QOL in MCS-12 compare with the LDQ group and control group. Among them, obese patients with liver depression and qi stagnation syndrome have the lowest MCS-12 scores. These initial findings show that the diagnosis of LDQ might help physicians identify obese patients with poor QOL.

The limitation of this study was that only four questions on symptoms experienced were designed for diagnosing or evaluating each obese TCM syndrome group; and hence, bias might exist. To our knowledge, there were no tools yet for detecting the different obese TCM syndrome groups. A self-reported symptom questionnaire was designed for this study as a diagnostic tool. Although validation was conducted, potential bias might exist.

In summary, obese patients with SHD in obese patients might have greater influence on the regulation of obesity-related hormone peptides, and obese patients diagnosed with LDQ have poor QOL. The concept of obese TCM syndrome diagnosis method might be applied to obesity health care. Related studies are worth more in-depth investigation in future.

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