UNIVERSITI PUTRA MALAYSIA

DETERMINANTS OF BONE MINERAL DENSITY AND EFFECT OF SOY ISOFLAVONES IN PREMENOPAUSAL WOMEN IN THE KLANG VALLEY

YVONNE TEE YEE SIANG

FPSK(p) 2013 14

DETERMINANTS OF BONE MINERAL DENSITY AND EFFECT OF SOY ISOFLAVONES IN PREMENOPAUSAL WOMEN IN THE KLANG VALLEY

By

YVONNE TEE YEE SIANG

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

June 2013

COPYRIGHT

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy

DETERMINANTS OF BONE MINERAL DENSITY AND EFFECT OF SOY ISOFLAVONES IN PREMENOPAUSAL WOMEN IN THE KLANG VALLEY

By

YVONNE TEE YEE SIANG

June 2013

Chair: Assoc. Prof. Zaitun Yassin, PhD

Faculty: Medicine and Health Sciences

Isoflavones, a class of phytoestrogens or plant-derived compounds with estrogenic activity found abundantly in soybeans and soy products, are purported to have protective effects on bone health. A 12-month randomized-control trial was conducted to determine the determinants of bone mineral density and effect of soy isoflavones on bone mineral density (BMD) among 73 non-osteoporotic premenopausal Chinese women.

The treatment group received 100 mg of soy isoflavones supplement daily containing approximately 43.09 mg (86.2%) of the isoflavones in aglycone form. Changes in BMD were assessed every 6 months using dual-energy X-ray absorptiometry (DEXA). Weight and height were measured using appropriate instrument and fat mass and lean mass were assessed by DEXA. Analysis on bone markers and several

biochemical indicators such as lipid profile was carried out. Dietary intake and selected lifestyle variables were also assessed.

At baseline, there was no significant difference between treatment and control group for their socioeconomic background, anthropometric measurements, dietary intake, biochemical parameters and physical activity level, except that the control group had higher baseline BMD at the Ward's triangle compared to the soy isoflavones group ($p<0.05$). The mean age of the subjects was 39.3 ± 5.0 years. Their mean body mass index (BMI) was 22.2 ± 3.4 kg/m^2 and their average body fat percentage and lean body mass were 33.9 ± 4.6% and 34.5 ± 4.4 kg, respectively. The mean BMD at the spine, total hip, femoral neck, and total body were 1.025 ± 0.118 g/cm^2, 0.876 ± 0.109 g/cm^2, 0.739 ± 0.110 g/cm^2, and 1.061 ± 0.755 g/cm^2, respectively.

The mean caloric and calcium intake were 1506 ± 427 kcal / day and 534 ± 347 mg / day, respectively. Their calcium intake only achieved 66.8% of the Recommended Nutrient Intake (RNI) of Malaysia. The mean metabolic equivalent score (MET) was 771.4 ± 926.1 min / week. On average, the serum levels of most biochemical indicators such as glucose, lipid profile, calcium, phosphorus, and magnesium were within normal range. Mean serum parathyroid hormone (PTH) was 36.1 ± 18.2 pg/ml; while mean serum beta-crosslaps was 0.21 ± 0.10 ng/ml. Conversely, mean serum osteocalcin (8.5 ± 4.2 ng/ml) was lower than the reference value.

Age at menarche was negatively correlated with BMD at the femoral neck ($r=-0.243$, $p<0.05$). Body weight and its related indices (BMI, lean mass, fat mass) were significantly correlated with BMD at all skeletal sites. None of the dietary and

physical activity factors were associated with BMD at various sites. Using the repeated measure ANOVA analysis, soy isoflavones supplementation had no effect on changes in BMD at all skeletal sites after 12 months. The findings of the study did not show any significant gain or loss in BMD from baseline in both the supplemented and control groups. Similarly, dietary intake, biochemical indicators and physical activity did not change significantly with time and between soy isoflavone and control group.

In conclusion, daily supplementation with 100 mg of soy isoflavones did not show a bone-sparing effect in healthy premenopausal women. Although the soy isoflavones tablets in this study were well-tolerated and did not result in any adverse effects, the long-term safety of very high supplemental doses of soy isoflavones is not yet known. Therefore, consumption of diets rich in soy and soy products may be the preferred option to gain the beneficial effects of isoflavones on bone health in both premenopausal and postmenopausal women.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

PENENTU KETUMPATAN MINERAL TULANG DAN KESAN ISOFLAVON SOYA KE ATAS WANITA PRA-MENOPAUS DI KLANG VALLEY

Oleh

YVONNE TEE YEE SIANG

Jun 2013

Pengerusi: Prof. Madya Zaitun Yassin, PhD

Fakulti: Perubatan dan Sains Kesihatan

Isoflavon, salah satu kelas fitoestrogen atau sejenis komponen yang terhasil dari tumbuh-tumbuhan yang mempunyai aktiviti estrogenik dan banyak terdapat dalam kacang soya atau produk soya, telah dikatakan mempunyai kesan perlindungan terhadap kesihatan tulang. Satu kajian reka bentuk kajian kawalan rawak yang mengambil masa 12 bulan telah dijalankan untuk menentukan penentu ketumpatan mineral tulang dan keberkesanan isoflavon soya terhadap ketumpatan mineral tulang di kalangan 73 wanita Cina pra-menopaus yang tidak mengalami osteoporosis.

Kumpulan eksperimen menerima 100 mg supplemen isoflavon soya setiap hari yang mengandungi 43.09 mg (86.2%) isoflavon dalam bentuk aglycone. Perubahan dalam ketumpatan mineral tulang diukur setiap 6 bulan dengan menggunakan X-ray absortiometri dua tenaga (DEXA). Berat badan dan ketinggian diukur dengan menggunakan alat yang sesuai. Analisis untuk penanda tulang dan beberapa

penunjuk biokimia seperti profil lemak badan telah dijalankan. Pengambilan makanan dan pembolehubah terpilih gayahidup juga dinilai.

Pada awal kajian, tiada perbezaan signifikan di antara kumpulan eksperimen dan kawalan dari segi latar belakang sosio-ekonomi, ukuran antropometri, pengambilan makanan, parameter biokimia dan tahap aktiviti fizikal, kecuali ketumpatan mineral tulang yang lebih tinggi dalam kumpulan kawalan pada Ward. Purata umur subjek adalah 39.3 ± 5.0 tahun. Purata Indeks Jisim Tubuh (IJT) mereka adalah 22.2 ± 3.4 kg/m^2, dan purata peratusan lemak badan dan jisim otot tanpa lemak mereka adalah 33.9 ± 4.6% and 34.5 ± 4.4 kg, masing-masing. Purata ketumpatan mineral tulang mereka pada tulang belakang, keseluruhan pinggul, leher femur, dan keseluruhan badan adalah 1.025 ± 0.118 g/cm^2, 0.876 ± 0.109 g/cm^2, 0.739 ± 0.110 g/cm^2, dan 1.061 ± 0.755 g/cm^2, masing-masing.

Min pengambilan kalori dan kalsium adalah 1506 ± 427 kcal dan 534 ± 347 mg sehari. Pengambilan kalsium mereka hanya mencapai 66.8% daripada Saranan Pengambilan Nutrien (RNI) Malaysia. Min skor metabolik setara (MET) mereka adalah 771.4 ± 926.1 min / minggu. Secara purata, paras serum kebanyakan penunjuk biokimia seperti glukosa, profil lipid, kalsium, fosforus, dan magnesium adalah dalam julat yang normal. Min serum hormon paratiroid (PTH) adalah 36.1 ± 18.2 pg/ml manakala min serum beta-crosslaps adalah 0.21 ± 0.10 ng/ml. Sebaliknya, min serum osteocalcin (8.5 ± 4.2 ng/ml) adalah lebih rendah rendah daripada nilai rujukan.

Usia mendapat haid dikaitkan secara negatif dengan ketumpatan mineral tulang pada leher femur ($r=-0.243$, $p<0.05$). Berat badan dan indeks yang berkaitan dengan berat badan (IJT, jisim otot tanpa lemak, jisim lemak badan) menunjukkan perkaitan yang signifikan dengan ketumpatan mineral tulang pada semua kawasan tulang. Tiada satu pun faktor diet dan aktiviti fizikal dikaitkan dengan ketumpatan tulang mineral. Dengan menggunakan ujian analisis repeated measure ANOVA, pemberian soya isoflavon tidak mempunyai kesan ke atas perubahan ketumpatan mineral tulang pada semua kawasan tulang selepas 12 bulan. Hasil kajian ini tidak menunjukkan sebarang peningkatan atau kehilangan jisim tulang berbanding dengan data pada awal kajian dalam kedua-dua kumpulan eksperimen dan kawalan. Begitu juga dengan pengambilan makanan, penunjuk biokimia dan aktiviti fizikal yang tidak berubah secara signifikan dengan masa dan antara kumpulan isoflavon soya dan kawalan.

Kesimpulannya, pemberian supplemen 100 mg soya isoflavon setiap hari tidak menunjukkan kesan perlindungan terhadap tulang dalam kalangan wanita pra-menopaus yang sihat. Walaupun wanita dalam kajian ini mempunyai toleransi yang baik terhadap tablet isoflavon soya dan tidak mengakibatkan apa-apa kesan buruk, keselamatan supplemen isoflavon soya dalam dos yang sangat tinggi untuk jangka masa panjang adalah belum diketahui. Oleh itu, pengambilan diet yang kaya dengan kacang soya dan produk soya mungkin merupakan pilihan yang lebih bijak untuk mendapatkan kebaikan isoflavon terhadap kesihatan tulang dalam kalangan kedua-dua wanita pra-menopaus dan menopaus.

ACKNOWLEDGEMENTS

This dissertation would not have been possible without the support and help of several individuals who contributed in one way or another to the completion of this study.

First and foremost, I would like to extend my heartfelt gratitude and appreciation to my supervisor Assoc. Prof. Zaitun Yassin for her guidance, support, and advice throughout the study. I am grateful for her encouragement as I hurdled all the obstacles in the completion of the research.

I am truly indebted and thankful to Assoc. Prof. Chan Yoke Mun, Assoc. Prof. Norhaizan, and Assoc. Prof. Zanariah for their unselfish and unfailing support, as well as their valuable advice.

A special thanks to Ms. Lesley who had gone the extra mile to assist me throughout the study period and we became friends in the end. I want to thank Dr JK Lee for giving me permission to commence the study at his clinic. I would also like to thank the support from the churches and Buddhist association. Especially, I would like to thank each of the ladies whose participation enabled me to complete the dissertation.

Last but not least, to my family members for their faith in me. Thank you all for the continuous love and patience. Words alone cannot express what I owe them for their unending support to help me survived the challenges.

This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

Zaitun Yassin, PhD
Associate Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Chan Yoke Mun, PhD
Senior Lecturer
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

Norhaizan Mohd. Esa, PhD
Associate Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

Zanariah Othman, PhD
Associate Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

_____
BUJANG BIN KIM HUAT, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date:

DECLARATION

Declaration by graduate student

I hereby confirm that:

- this thesis is my original work
- quotations, illustrations and citations have been duly referenced
- this thesis has not been submitted previously or concurrently for any other degree at any other institutions
- intellectual property from the thesis and copyright of thesis are fully-owned by Universiti Putra Malaysia
- written permission must be obtained from supervisor and Deputy Vice-Chancellor (Research and Innovation) before thesis is published in book form
- there is no plagiarism or data falsification/fabrication in the thesis, and scholarly integrity was upheld as according to Rule 59 in Rules 2003 (Revision 2012-2013). The thesis has undergone plagiarism detection software

Signature: _____ Date: _____

Yvonne Tee Yee Siang (GS 19763)

Declaration by Members of Supervisory Committee

This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in Rule 41 in Rules 2003 (Revision 2012-2013) were adhered to.

Signature: _____
Assoc. Prof. Zaitun Yassin

Signature: _____
Dr. Chan Yoke Mun

Signature: _____
Assoc. Prof. Norhaizan Mohd. Esa

TABLE OF CONTENTS