



Indonesian Menopause Society Member Country Session

Date: Monday 27 September 2010

Time: 07.30am – 08.30am

Session Chair: To be announced

Session Topics:

Dr M D Sustrisno

- Effect of Genistein to the expression of estrogen receptor, estrogen receptor β , cAMP and apoptosis on oxidative stress in human endothelial cell culture

Dr M Sjarief Darmasetiawan

- MEN-QOL (Menopause Quality of Life) : Which measurement is appropriate ?

Dr Ratsmawan

- The Role of Leptin on estradiol and Bone Mass Density of Post Menopausal Women

Dr R. Amran

- Effectiveness of the use of Isoflavone capsules to hot flushes in menopause women in RSMH Palembang.

Dr T Agoestina

- Polymorphism -351 XbaI A/G and -397 PvuII T/C of ER α gene, expression of MMP-9 and TIMP-1 with irregular bleeding in postmenopausal women using hormone therapy (HT).
 - Polymorphisms of gene ER α -351 XbaI A/G and -397 PvuII T/C, and the balance of MMP-9 and TIMP-1 productions related to postmenopausal bleeding receiving HRT. (Dr. T. Agoestina, .OG, M.H - Bandung).
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ABSTRACTS

Effect of Genistein to the Expression of Estrogen Receptor α , Estrogen Receptor β , Camp and Apoptosis on Oxydative Stress in Human Endothelial Cells Culture

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Objective : to determine the effects of doses of Genistein to the level of apoptosis and expression estrogen receptor α (ER α), estrogen receptor β (ER β), and cAMP on stress oxidative human endothelial cell culture.

Setting : Biomedical and Pharmacology Department of Brawijaya University Faculty of Medicine, Malang, Indonesia

Design : Experimental study on Human Endothelial cell Culture (HUVEC Culture)

Material and Methods : Culture of human umbilical vein endothelial cells (HUVEC) had been divided to be seven Group. Group I is control group (without intervention), Group II is exposed with 33mM of glucose (oxidative stress group), Group III is group II added with 17 β estradiol 10 nM, Group IV is group II added with genistein 2,5 μ m, Group V is group II added with genistein 5 μ m, group VI is group II added with genistein 7,5 μ m, and group VII is group II added with genistein 10 μ m.

Result : The expression of ER α is similar in group III, group V, group VI and group VII in all duration of evaluation, the expression of ER β is similar in group III, IV, V, VI and VII, the expression of cAMP is similar in group III, VI and VII, and number of apoptotic endothelial cell similar in group III, V, VI and VII.

Conclusion: the dose of genistein had significantly correlate with expression of ER α , ER β , cAMP and number of apoptotic cells in oxidative stress endothelial cell culture.

MEN-QOL (Menopause Quality of Life) : Which measurement is appropriate ?

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Objective

The standard research method for measuring and collecting information on the prevalence and severity of climacteric symptoms was often using a variety of tools comprises a check list of symptoms. Symptoms represent a subjective expression of manifestation of some underlying physical, psychological or social dysfunction^{1,2}. Therefore every instrument being used for measuring so called a quality of life should be a reliable and valid measures. The techniques developed to construct such measures must fulfill four criteria as follows : 1. That the scale have been constructed on the basis of a factor analysis 2. It consists of several subscales which measuring a different aspect of specific symptomatology 3. It possessed psychometric properties, and 4. It has been standardized using adequate populations of women. There are 3 standardized Menopause-Specific QOL scales commonly used for menopausal research in Indonesia, known as Greene climacteric scale, Menopausal Symptom list, and Menopause-Specific QOL Questionnaire. Kupperman index is not included here since it neither contains of a simple symptoms inventory without being standardized nor apply the psychometric methodology properties¹. The aim of this study is to compare these three instruments and envisage for having a standard scales tool for menopause research.

Design

As an initial step; with the exceptional of Menopause-Specific Quality of Life questionnaire which had already translated and being used during the previous PAM (Pan Asia-Pacific) study; the two original questionnaire was translated to Indonesian language by a professional translator as a semantic expert. Fifty respondents were recruited to the study. They were instructed to fill scale instrument as a self-assessment in a 3 separated week for each of the three instruments. A team consist of two psychiatrist were involved for re-accessing the proper expression of respondents answer. A proper statistical analysis was performed for analyzing the data.

Conclusion

This ongoing study showed that Menopause-Specific Quality of Life Questionnaire (0.55-0.85 Reliability of subscales) which develop by Hilditch et al seem more practical to be implemented at least for Indonesian women population. Further study involving more respondent is required.

The Role of Leptin on estradiol and Bone Mass Density of Post-Menopausal Women
Ratsmawan H.S, Hendarto H, Darmosoekarto S
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Background

Leptin is hormone with diverse range of local and systemic physiological functions produced in adipose tissues and secreted into the peripheral blood and also correlates well with body weight and adiposity. Estradiol has effects on food intake and body weight that are in the same direction as leptin. Serum estradiol also has positively correlation to bone density.

Objective

To evaluate whether leptin had role on estradiol and the bone mass density in postmenopausal women.

Methods

Serum leptin and estradiol of 17 non obese postmenopausal women and 17 non-obese nonmenopausal women as a control were evaluated using ELISA technique. Bone mass density value was evaluated using Dual energy X-ray absorptiometry (DEXA). All women had not taken any hormone, calcium and corticosteroid medication at least 6 months before the study. They had no established endocrinologic diseases (e.g. Hyperthyroidism, Cushing's disease, diabetes mellitus) or rheumatologic pathologies (e.g. rheumatoid arthritis, ankylosing spondylitis),

Results

Serum leptin concentration was higher in postmenopausal women ($18,41 \pm 16,61$) compared with nonmenopausal women ($9,27 \pm 3,01$) ($p=0.02$). BMD in postmenopausal women was lower ($1,00 \pm 0,16$) than nonmenopausal women (1.13 ± 0.12) ($p=0.002$). The median concentration of estradiol in postmenopausal women was lower (<20) than menopausal women ($27,70$) ($p=0.0008$). There were no significant correlations between leptin and estradiol concentration ($r= 0.241$, $p = 0.352$), and also between leptin concentration and bone mass density in postmenopausal women ($r=0.625$, $p=0.004$).

Conclusion

The increase concentration of serum leptin has no correlation on estradiol and bone mass density in postmenopausal women.

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Differences Effects Of Isoflavone And Placebo In Reducing Hot Flushes Menopausal Women In Palembang

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Background

Hot flushes is the most vasomotor symptoms suffered by most women at age of menopause. Around three quarters of menopausal women experience symptoms of hot flushes in her life. These symptoms usually appear 1 -2 years before menopause and will continue for six months until the next five years. Hot flushes in menopausal women will affect the ability to work, disrupt the social life, sleep pattern and daily activities. Effort to reduce symptoms for menopausal women is by giving hormone therapy; administration of estrogen with or without progestin, or selective estrogen receptor modulators (SERMs) such as raloxifene and tamoxifen. besides that, hormone therapy should also be done in the long term even for life so that it will cause the problems in compliance of drug using and higher costs. One of the most widely studied phytoestrogens are isoflavones, a 17β -oestradiol which are weak estrogens and SERMs natural. Isoflavones are widely used derived from soy isoflavone extract in capsules, tablets and liquids.

Objective

Study aims to know the differences effect of isoflavones and placebo in reducing hot flushes complaints of menopausal women. Overall benefits of the research is expected Isoflavones to be considered as alternative therapy in managements of menopausal complaints and can improve quality of life of women during this period with relatively affordable cost.

Design and method

This study is randomized clinical trial to isoflavon 2x40mg group and placebo group during 12 weeks. Was performed from September 2007 until June 2008 at Muhammad Hoesin Hospital Palembang, Dempo Public Health Centre , and Merdeka Public Health Centre Palembang. There were 90 sample in age 45-55 years old that meet the inclusion criteria and participated to this study.

Results

From the results, the mean age of subjects in the isoflavone group for $50,75\pm 2,31$ years old and $51,10\pm 2,25$ years old in placebo group. The mean menopausal age of isoflavone group for $48,12\pm 1,57$ years old and $48,30\pm 1,53$ years old in placebo group. The majority of subject had a normal body mass index (BMI= 18,5-25), as many as 30 subject (75,0%) in isoflavon group and 28 subject (70%) in placebo group. The biggest subject distribution of isoflavon group is more than 2 parity as many as 29 subject (72,5%), likewise in placebo group 23 subject (67,5%). Overall, subject characteristics of both group before intervention was found on the entire body of 18 subjects (45,0%) in the isoflavon group and 16 subjects (40%) in placebo group.

Conclusions

Result showed there were significant differences in the effect of isoflavone and placebo in reducing hot flushes complaints of menopausal women. Frequency of hot flushes decrease significantly in the first two weeks up to two weeks of sixth. The mean frequency of hot flushes at two weeks of sixth is 9.60 ± 4.18 times in two weeks (\pm once a day) in isoflavone group and 17.98 ± 5.51 times in two weeks (\pm twice a day) in placebo group ($P<0.05$)

This is also followed by a decrease in the duration and severity of hot flushes in the group of isoflavone. In the two weeks of sixth, the average duration of hot flushes isoflavone group 2.20 ± 1.01 minutes versus 5.70 ± 3.03 minutes in group placebo and have proven statistically significant. Overall in isoflavone group, there were 32 subjects with mild degrees of hot flushes and 8 subjects with moderate hot flushes. While in the placebo group, there were 17 subjects with mild degrees of hot flushes and 23 subjects with moderate degrees of hot flushes.

Polymorphism -351 XbaI A/G and -397 PvuII T/C of ER α gene, expression of MMP-9 and TIMP-1 with irregular bleeding in postmenopausal women using hormone therapy (HT).

Agoestina, Dr. Tina, Sp. OG, M. Kes (Bandung)¹

The mechanisms of postmenopausal HT-related bleeding are poorly understood. Functionally significant polymorphisms in ER gene XbaI and PvuII maybe associated with the risk of endometrial bleeding in HT postmenopausal women through regulation of estrogenic effect at the cellular level. Endometrial matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs) are believed to regulate bleeding during the normal menstrual cycle. This study to elucidate the association of polymorphisms -351 XbaI A/G, -397 PvuII T/C of ER α gene and expression of MMP-9 & TIMP-1 in endometrium at the onset of bleeding during postmenopausal HT. A case-controlled study was conducted in MCH Sukajadi Bandung, May'09 – February'10. Women were divided into two groups: 1) 20 women with bleeding/btb as the case group and 2) control, 20 women with spotting. Polymorphisms -351 XbaI A/G, -397 PvuII T/C of ER α gene were assayed by the method of PCR-RFLP and Immunohistochemical examinations were conducted for analysis of MMP-9 & TIMP-1 expression in the endometrial stroma and glands.

The proportion of genotype/allele of polymorphisms -351 XbaI A/G, -397 PvuII T/C of ER α gene in bleeding group were significantly different from those spotting control (X² trend = 4,101; p = 0,043) and (X² trend = 4,951; p = 0,026) respectively. OR XbaI allele G, -397 PvuII allele C of ER α gene (2,25 dan 3,11) each, higher than allele A and allele T to cause bleeding/btb. MMP-9 and TIMP-1 expression in stroma and gland between endometrial bleeding in HT recipients, only the distribution (%) of each in the stroma were found significantly different (p = 0,045). OR for MMP-9 in stroma and gland was higher risk for the development of bleeding/btb in all staining categories of intensity and distribution compared to negative staining. OR=9 for MMP-9 in distribution (%) stroma was higher risk compared to negative staining. Intensity and distribution of TIMP-1 showed only in stroma, the weak intensity (OR=5,62) were correlated with higher susceptibility of endometrial bleeding in HT users compared to negative intensity, and other distribution of TIMP-1 showed lower risk of bleeding. Multiple regression logistic analysis to correlate genotype polymorphisms XbaI and PvuII of ER α gene and expression of MMP-9 & TIMP-1, in stroma and gland with bleeding. Genotype AG and GG of XbaI were higher risk of the development of bleeding than genotype AA; TIMP-1 expression was higher risk of the development of bleeding than negative expression, in stroma and gland. Genotype TC and CC of PvuII were higher risk to cause bleeding than genotype TT.

In summary, XbaI G, PvuII C alleles of ER α genes and expression of MMP-9 & TIMP-1 in endometrial stroma and gland during HT in postmenopausal women appeared to convert an increased risk of uterine bleeding.