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Tarikh : 25 September 2002

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PEKELILING KETUA PENGARAH KESIHATAN BIL. 8/2002

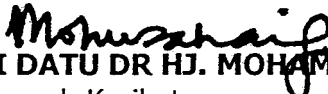
Pendirian Kementerian Kesihatan Malaysia Berhubung Dengan Isu Terapi Gantian Hormon (*Hormone Replacement Therapy*) Dan Laporan Penyelidikan 'Women's Health Initiative' (WHI)

Adalah dimaklumkan, penerbitan hasil penyelidikan Women's Health Initiative (WHI) yang mendapati pertambahan risiko penyakit koronari, strok dan kanser payudara di kalangan wanita Amerika yang mengambil rawatan Terapi Gantian Hormon (premarine 0.625 mg/day dan medroxyprogesterone acetate (provera) 2.5 mg/day) telah menimbulkan kekeliruan dan kontroversi berhubung dengan penggunaan Terapi Gantian Hormon secara amnya.

2. Sehubungan itu, bersama-sama ini disertakan salinan pendirian Kementerian Kesihatan Malaysia berhubung perkara tersebut untuk makluman dan tindakan yang sewajarnya.

Sekian, terima kasih.

'BERKHIDMAT UNTUK NEGARA'


(TAN SRI DATU DR HJ. MOHAMAD TAHA BIN ARIF)
Ketua Pengarah Kesihatan
KEMENTERIAN KESIHATAN MALAYSIA

s.k.

Timbalan Ketua Pengarah Kesihatan (Kesihatan Awam)

Timbalan Ketua Pengarah Kesihatan (Perubatan)

Timbalan Ketua Pengarah Kesihatan (Sokongan dan Teknikal)

Ketua Jabatan O & G

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Hospital Kangar

Hospital Alor Setar

Hospital Pulau Pinang

Hospital Ipoh

Hospital Tengku Ampuan Rahimah, Klang

Hospital Selayang

Hospital Seremban

Hospital Melaka

Hospital Sultanah Aminah

Hospital Tengku Ampuan Afzan

Hospital Terengganu

Hospital Kota Bharu

Hospital Queen Elizabeth

Hospital Kuching

Hormone Replacement Therapy (HRT) and Women's Health Initiative (WHI) Report – The Position of The Ministry of Health Malaysia

The report of the Women's Health Initiative (WHI) trial on hormone replacement therapy (HRT) in postmenopausal women published in the Journal of the American Medical Association (JAMA) on the 17th July 2002 has raised concerns regarding its use. The Ministry of Health, related professional bodies and non-government organizations met on 20th August 2002 to discuss their stand on the findings of WHI.

This paper briefly describes the salient features of the WHI's study, its key findings with risks towards specific diseases and its limitations. Based on these, the paper makes specific recommendations which are to be noted and acted upon by health care providers.

The Study

The WHI study was designed to assess the major benefits and risks of the most commonly prescribed continuous combined HRT (conjugated equine estrogen 0.625 mg/day and medroxyprogesterone acetate 2.5 mg/day) among postmenopausal women in the United States. The women selected were between ages 50 and 79 years with a mean age of 63 years. In this study, 16,608 women with intact uterus at baseline, were recruited in 1993 – 1998 and they were assigned to receive the continuous combined HRT or placebo (sugar pills).

The trial was planned to last 8.5 years, that is, to be completed in the year 2005. However, it was halted after 5.2 years because of an observed increased risk of cardiac disease, namely heart attacks, stroke, deep vein thrombosis and pulmonary embolism; and invasive breast cancer. The study also reported benefits in the reduction of hip fractures and colon cancer.

Findings

In summary, the results of the study indicated that for every 10,000 women taking the continuous combined HRT, there would be:

- 7 more women with heart attacks
- 8 more women with strokes
- 8 more women with breast cancer
- 18 more women with blood clots
- 6 fewer colorectal cancers
- 5 fewer hip fractures
- fewer fractures in other bones

Table 1 summarises the findings in a simplified statistical manner.

Table 1. The relative risks of getting diseases among 10,000 women who are on continuous combined HRT as compared with 10,000 women who are on placebo.

| Diseases | Combined HRT *(CEE and MDA) (number of cases) | Placebo (number of cases) | Relative Risk | |
|--------------------|---|------------------------------|---------------|--------|
| Heart attacks | 37 | 30 | 1.29 | [29%] |
| Strokes | 29 | 21 | 1.41 | [41%] |
| Breast cancers | 38 | 30 | 1.26 | [26%] |
| Blood clots | 34 | 16 | 2.13 | [213%] |
| Colorectal cancer | 10 | 16 | 0.63 | [-37%] |
| Hip fractures | 10 | 15 | 0.66 | [-34%] |
| Endometrial cancer | 5 | 6 | 0.83 | [-17%] |
| Deaths | 52 | 53 | 0.92 | [-8%] |

*CEE – conjugated equine estrogen
MDA – medroxyprogesterone acetate

Limitations of the Study

1. Profile of study subjects

It should be noted that the report was among American women whose average age was older (63 years) and the majority were overweight. The mean age is far above the age that HRT should be started for prevention purposes. About 30% already had pre-existing cardiovascular risk factors. Other recent studies showed that older women with established cardiac disease should not be started on combined continuous HRT. About 40% of the study patients were ex-smokers and 10% of the patients were still smoking during the study period.

2. Drop-out from the study

It should be pointed out that there were 40% drop-out rate of women receiving HRT mostly due to the problem of vaginal bleeding, and another 3% of this group had to undergone hysterectomy.

3. Hormone preparation and regimen

The trial tested only one regimen of continuous combined HRT, which is conjugated equine estrogen 0.625 mg/day, and medroxyprogesterone acetate 2.5 mg/day. The results do not necessarily apply to other dosages of the drugs or drugs taken cyclically. The results also do not apply to other formulations of oral estrogens and progestins or other routes of administration e.g. transdermal. The effects of progestin may be important for breast cancer and atherosclerotic disease.

Recommendations of the Ministry of Health

Based on the above, the Ministry of Health together with relevant parties (*see page 4*) make the following recommendations to be noted by health care providers:

1. General

- 1.1 Health care providers are to recognise that what have been highlighted by the media are the relative risks to the above diseases, and that the absolute risks although significant are small.
- 1.2 Women currently taking HRT are advised not to panic and have undue fear. They should be counseled by their doctors to weigh the benefits and the risks of continuing therapy. They are also to be informed of the many preparations and regimens of HRT available in Malaysia.
- 1.3 All women prescribed with HRT should consult their doctors and undergo regular follow-up and health screening. Prescribing HRT is an individualized and personal decision made after consultation between a woman and her doctor and taking into account a woman's individual benefits and risks from such use.

2. HRT for treating menopausal symptoms

The use of HRT whether cyclical or continuous for the purpose of relieving menopausal symptoms is justified since the benefits outweigh the risks.

3. HRT for the preventing cardiovascular diseases

- 3.1 The combined continuous therapy of conjugated equine estrogen and medroxyprogesterone acetate should not be initiated or continued for

cardiovascular disease prevention only. However, a combined therapy of other estrogen and other progestin, a low dose HRT and transdermal therapy can be considered to be used.

- 3.2 HRT should not be used for the sole purpose of preventing a second attack or death among women with established heart diseases.
- 3.3 Women at risk of cardiovascular disease who wish to discontinue HRT should consider dietary and lifestyle changes (weight loss, regular exercise, stop smoking) as well as the use of drugs to lower cholesterol and blood pressure.

4. HRT for managing osteoporosis

Women at risk of osteoporosis who wish to discontinue HRT should be evaluated and consider the use of alternative therapies such as calcium, biphosponates and the selective estrogen receptor modulators (SERM).

Conclusion

For many women, menopause brings many uncomfortable symptoms as the body produces less estrogen hormone. Hot flushes, sleeplessness and vaginal dryness prevent some women from carrying on the day-to-day functions. Thus women should not abandon HRT altogether. The benefits should be evaluated whether they outweigh the risks. We need to make decisions about HRT on an individual basis. For many, the decision will be straightforward with potentials for significant benefits for example for symptomatic relief and in many areas. For some others, the decision will be much more difficult requiring a careful balance of the known benefits and potential risks which can be achieved after a careful consultation between the woman and the attending doctor.

List of Participating Organizations:

1. Ministry of Health Malaysia (MOH)
2. Private Medical Practitioners Association
3. National Population and Family Development Board (NPFDB)
4. Federation of Family Planning Associations Malaysia (FFPAM)
5. Obstetrical & Gynaecological Society of Malaysia
6. Malaysia Medical Association (MMA)
7. Malaysian Menopause Society (MMS)

Drma/nb/19.9.02