



Indian Menopause Society

Guideline Number 10 : February 2011

Hormone Therapy and Cardiovascular Disease

Introduction : The burden of cardiovascular diseases(CVD) is rising in India. The estimated prevalence of coronary heart disease is around 3–4% in rural areas and 8–10% in urban areas representing a two-fold rise in rural areas and a six-fold rise in urban areas over the last decade.¹

The incidence of CVD in Indian women has been noted to have significantly risen. The projected deaths from CVD by 2020 are estimated to be 42% of the total deaths². There is an increased prevalence of metabolic syndrome; a risk factor for CVD. After the menopause, the risk of CVD increases, regardless of the age at which this occurs.

Menopausal hormone therapy (HT) once seemed the answer for many of the conditions women face as they age. It was thought that hormone therapy could prevent CVD, osteoporosis, and cancer, while improving women's quality of life. But beginning in July 2002, findings emerged from the Women's Health Initiative (WHI) study³ that showed this was not so. In fact, long-term use of hormone therapy poses serious risks and may increase the risk of heart attack and stroke.

Problems with WHI : The WHI concluded that hormone therapy is not a viable intervention for primary prevention of CHD. However, the WHI did not study the appropriate population in the appropriate time period to establish that hormone therapy does not exert a primary preventive effect on the risk of coronary heart disease. The increase in cardiac events demonstrated in the first year in the WHI trial could have been because of inclusion of older women (mean age 63.3years) and an at-risk population. This observation is similar to that from the Heart and Estrogen/ Progestin Replacement study (HERS) on women with documented pre-existing coronary heart disease (CHD) where mean age was 67years.⁴

The other objection to WHI was the type and route of delivery of the progestin. Recent studies support the use of micronized progesterone, drospirenone and LNG-IUS in HT to obtain more favourable effects on lipids, blood pressure and weight.⁵

Recent Analysis of WHI : This has shown that the apparent increased risk of CHD is not statistically significant. Estrogen alone therapy in the age group 50-59 years was associated with significantly less coronary calcification. Early harm in the form of more coronary events during the first 2 years of HRT was not observed in the early menopausal period and there may even be some cardiovascular protection. The number of CHD events decreased with duration of HRT in both WHI clinical arms.⁶

Clinical Recommendations for Prevention of CVD

The latest evidence based update for prevention of CVD in women has been provided in 2007 by American Heart Association.⁷ This is based on risk classification as shown below.

Classification of CVD Risk in Women

Risk status	Criteria
High risk	Established coronary heart disease or vascular disease Diabetes mellitus
At risk	1 major risk factor for CVD, including smoking, poor diet, physical inactivity, obesity, family history of premature CVD, Hypertension, Dyslipidemia, Metabolic syndrome
Optimal risk	Framingham global risk < 10% and a healthy lifestyle with no risk factors

Life style interventions have been recommended for all risk categories. In addition, aspirin should be considered in women at risk along with drug interventions for control of hypertension, dyslipidemia and diabetes. Aggressive intervention and specialist referral is recommended in women who are deemed as high risk.

Hormone therapy (HT) & CVD

While questions remain, the findings from the WHI suggest that estrogen alone or with progestin should not be used to prevent heart disease particularly in women at high risk for CVD. Other ways of preventing heart attack and stroke, including lifestyle measures such as weight reduction, exercise, proper diet, avoidance of excessive alcohol and stress, cessation of smoking and introduction of statins, aspirin and anti-hypertensives should be advocated where necessary.

Further analysis of randomized, controlled and prospective studies indicates that early administration of hormone therapy in younger postmenopausal women can afford protection against cardiovascular disease, while initiation of therapy at an older age, after 10 years without endogenous estrogen, is harmful.⁸

HT needs to be used appropriately and it is suggested that women in the early post-menopausal years should have the option of using HT for symptom relief. Detailed counseling needs to be done. Younger women should be informed that WHI study data need not necessarily apply to women in their 50s. If prescribed, HT should be used in a low dose and for a short duration.¹ It is unclear at present whether there is an increase in ischemic stroke with standard HT in healthy women aged 50-59, nevertheless, even if statistically increased, the low prevalence of this occurrence in this age group makes the attributable risk extremely small. The increased risk of venous thrombosis with oral HT also is a rare event in that the background prevalence is low in a healthy woman under 60 years of age.

Window of Opportunity: The results from studies in younger women over the last few years support an emerging theme that a healthy endothelium is needed to respond to estrogen. In postmenopausal women, the vasodilatory effects of estrogen dissipate with increasing age. By the time, the endothelium is involved with atherosclerosis, it is too late for estrogen to exert a beneficial effect. Recent reports make an argument that the optimal approach to postmenopausal hormone therapy is to start treatment close to the menopause, avoiding a significant period of exposure to low estrogen levels prior to beginning therapy. Benefits of HT in preventing atherosclerosis occurs only when the therapy is started during the early postmenopausal years, known as the “window of opportunity”, before advanced atherosclerosis develops.

The International Menopause Society issued a Consensus Statement after a workshop on CVD and Hormone Replacement Therapy (HRT) in 2009.⁹ The consensus of the Workshop was that HRT can be given to women around the age of natural menopause without increasing the risk of coronary heart disease and may even decrease the risk in this age group. HRT is not contraindicated in women with hypertension and, in some cases, HRT may even reduce blood pressure. HRT is contraindicated in women with a history of myocardial infarction, stroke, or pulmonary embolism.

Primary Cardioprotection

HT is not recommended for primary cardioprotection. However, if used for symptom relief, it can have beneficial effects on CHD if started in younger women closer to menopause.

Risk for heart disease, stroke, osteoporosis, and other conditions may change as the person ages, so health should be reviewed regularly. New treatments that are safe and effective may become available.

Secondary Cardioprotection

The results of secondary prevention trials provide a reasonably solid basis not to recommend postmenopausal hormone therapy for women with existing atherosclerosis in the anticipation of preventing future cardiovascular events.^{4,10}

Conclusion : Menopausal hormone therapy was once thought to lower the risk of heart attack and stroke for women at risk. Research now shows that Hormone therapy should not be used for the primary or secondary prevention of CVD in women. However, in recently menopausal women, who are below the age of 60 years, HT may be used for symptom relief after appropriate work up and counseling. These women may get some protection against CVD.

References

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