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AWARD 2005

Type of HRT Is Key With Regard to Myocardial Infarction Risk (MI)

The WHI study found an increased risk of coronary heart disease and stroke in women using HRT, resulting in premature termination of the study, but it is not clear whether the duration, dosage, and type of HRT affect the risk of MI (Update issues 34 & 54) .

A longitudinal cohort study of healthy Danish women (aged 51-69) using the Danish National Registry to examine the role of HRT and type, dose, regimen, and duration of the therapy on risk of MI among postmenopausal women has been recently reported. Women were observed from 1995 to 2001. 4947 events of MI were recorded over the follow-up period, for a total of 698,098 women with 2,952,635 women-years of observation. 74% of women did not use HRT, 7% were former users, and 19% were current users.

Findings

There is no overall increase in MI risk with use of HRT in postmenopausal women, but an increase in risk is noted in younger women aged 51 to 54 years. The estimates of MI risk with HRT use were similar to previously documented

No increased risk of MI was found with unopposed estrogen, cyclical combined HRT, or tibolone. A significantly lower risk of MI was found with dermal routes when the risk of MI was reduced by 38%, and for vaginal application, by 44%, compared with oral unopposed estrogen therapy (This is the first time vaginal preparations of estrogen have been tested in a large observational study). The highest risk (increase by 35%) of MI was found with the continuous combined HRT compared with women who never used HRT

Risk of MI in the various HRT categories

HRT status	MIs	Rate per 1000 women-years	Adjusted RR
By regimen			
Never used	3596	1.73	1.00
Estrogen	288	1.60	0.94
Long cycle combined	34	1.30	1.07
Cyclic combined	244	1.11	0.92
Continuous combined	244	2.07	1.35*
Tibolone	24	1.23	0.80
By route			
Never used	3596	1.73	1.00
Oral estrogen	264	1.78	0.98
Dermal estrogen	24	0.77	0.62*
Oral combined	523	1.46	1.08
Dermal combined	23	0.91	0.95
Vaginal	69	1.00	0.56*

*Significant RRs

There was no association between estrogen dosage and MI risk. There was no increased risk of MI with type of estrogen or progestogen used. Duration of HRT use did not affect MI risk, with RR being 1.06, 1.03, and 0.99, respectively, for short-, middle-, and long-term use.

There were no significant interactions between use of hormones and concomitant use of medications for diabetes or hypertension. Pre-existing conditions did not influence the risk of MI with HRT use

Conclusion

The study does not change indications and recommendations about the duration of HRT. The main message is that

* When combined HRT is indicated for a woman (especially aged 51 to 54), then a cyclical regimen or tibolone should be preferred.
* When oestrogen only HRT is indicated then application of estrogen via the skin or vagina is associated with the lowest risk of MI
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Reference: Lokkegaard E, Andreasen AH, Jacobsen AK, et al. Hormone therapy and risk of myocardial infarction: a national registry study. *Eur Heart J* 2008; DOI:10.1093/eurheartj/ehn408. Available at: http://eurheartj.oxfordjournals.org