Oral estrogen hormone therapy linked to increased risk of gallbladder surgery in menopausal women

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Oral estrogen therapy for menopausal women is associated with an increased risk of gallbladder surgery, according to a large-scale study of more than 70 000 women in France published in *CMAJ* (*Canadian Medical Association Journal*)

Women who took estrogen therapy through skin patches or gels did not appear to be at increased risk.

Gallstone disease is common in developed countries, and women over age 50 are most at risk. Other risk factors include obesity, diabetes, high cholesterol, poor diet and having given birth to two or more children.

A large study of 70 928 menopausal women in France between 1992 and 2008 looked at whether hormone therapy increased the risk of gallbladder surgery (cholecystectomy) for complications of gallstones. In France, hormonal therapy is usually administered topically rather than orally. North America and the United Kingdom prefer oral hormone therapies.

"In this large French prospective cohort study, we found that the risk of cholecystectomy was increased among women exposed to oral estrogen regiments for menopausal hormone therapy, especially oral regimens without progestagen," writes Dr. Antoine Racine, Institut national de la santé et de la recherche médicale (INSERM) and Université Paris Sud,

with coauthors. "Other types of menopausal hormone therapy were not associated with an increased risk of cholecystectomy."

"Complicated gallstone disease should be added to the list of potential adverse events to be considered when balancing the benefits and risks associated with menopausal hormone therapy," the authors conclude.

In a related commentary, Dr. Bette Liu, Faculty of Medicine, University of New South Wales, Sydney, Australia, writes that the findings of this study support current recommendations for minimizing doses and duration of hormone therapy for menopausal symptoms. However, if hormone therapy is considered necessary, transdermal formulations (such as patches or gels) may have fewer adverse effects than oral formulations.

"Unfortunately there are no large clinical trials comparing transdermal and oral therapies, and such trials will probably never be conducted," she writes. "Evidence to guide recommendations on the best route of hormone administration for individual women and prescribers will thus be limited to the growing volume of observational data. These data suggest that the overall risk–benefit profile of transdermal menopausal hormone therapy makes it a more attractive option than oral therapies."

More information: www.cmaj.ca/lookup/doi/10.1503/cmaj.121490
Commentary: www.cmaj.ca/lookup/doi/10.1503/cmaj.130004

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