TITLE: Conjugated Versus Singular Estrogens for the Management of Menopausal Symptoms: Comparative Clinical Effectiveness and Safety

DATE: 29 October 2009

RESEARCH QUESTION:

What is the comparative clinical effectiveness and safety of conjugated estrogens versus singular estrogens for the management of menopausal symptoms in women?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, the Cochrane Library (Issue 4, 2009), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between 2004 and October 2009. Filters were applied to limit the retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials (RCTs), and controlled clinical trials (CCTs). Internet links were provided, where available.

Only RCTs and CCTs containing at least one study arm comparing the clinical effectiveness of conjugated estrogens with other estrogens when used alone for the management of menopausal symptoms were considered for inclusion. RCTs and CCTs comparing different estrogens in combination with progestins were excluded.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

RESULTS:

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by RCTs and CCTs.

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Three systematic reviews and meta-analyses and three RCTs were identified pertaining to the comparative clinical effectiveness and safety of conjugated estrogens versus singular estrogens for the management of menopausal symptoms in women. No relevant health technology assessments or CCTs were identified. Additional information, including studies evaluating surrogate risk markers for cardiovascular events, has been included in the appendix.

OVERALL SUMMARY OF FINDINGS:

Three relevant systematic reviews and meta-analyses\(^1\text{-}^3\) were identified. Of the three systematic reviews, one found statistically significant differences between conjugated and singular estrogen therapies for safety outcomes.\(^1\) This review compared the effectiveness, safety, and acceptability of estrogen products for postmenopausal women with vaginal atrophy. Conjugated estrogens and singular estrogen products appeared to be equally effective for the symptoms of vaginal atrophy. In the analysis that compared conjugated estrogen creams and singular estrogen products, adverse events such as uterine bleeding, breast pain, perineal pain, and endometrial overstimulation were significantly more common in women using conjugated estrogen creams than in those using tablets or vaginal rings containing estradiol. Most women appeared to favour the estradiol-releasing vaginal ring over other estrogen products. Results from a second systematic review found that the type of estrogen treatment (conjugated or estradiol) had no effect on the risk for stroke in patients receiving hormone replacement therapy.\(^2\) The third systematic review compared the short-term effectiveness of conjugated equine estrogen with 17beta-estradiol for the management of hot flashes.\(^3\) Results did not show a significant difference in effectiveness or adverse effects between the two types of estrogen.\(^3\)

Of the three identified RCTs, one found significant differences for the relief of menopausal symptoms between conjugated and singular estrogens\(^4\) and two did not.\(^5,6\) One trial compared the effects of oral conjugated estrogen, intranasal estradiol hemihydrate, and percutaneous gel estradiol hemihydrate on psychological symptoms in surgically menopausal women.\(^4\) While no significant differences were found between the different types of estrogen for improved menopausal symptoms and anxiety after one year of therapy, oral conjugated estrogen was significantly more effective than both intranasal and percutaneous gel estradiol hemihydrate for depressive mood.\(^4\) In another RCT, after one year of therapy, oral conjugated estrogens and transdermal estradiol were found to be equally effective in reducing menopausal symptoms based on a self-administered quality of life questionnaire.\(^5\) A third RCT found no significant difference between the number and severity of vasomotor and urogenital symptoms in postmenopausal women treated with oral conjugated equine estrogens, oral estradiol acetate, or oral micronized estradiol.\(^6\)

Overall, evidence from systematic reviews\(^1,^3\) and RCTs\(^5,^6\) indicated comparable clinical effectiveness for the relief of vasomotor and urogenital symptoms when conjugated estrogens were compared with other estrogen products. Results from one RCT indicated that oral conjugated estrogen may be more effective than other formulations of estradiol for the management of depressive symptoms but there were no significant differences for other psychological symptoms such as anxiety.\(^4\) While conjugated estrogen creams were shown to have more adverse effects than estradiol rings and tablets in one systematic review,\(^1\) comparable adverse events were reported for conjugated and singular estrogens in the other two systematic reviews.\(^2,^3\)
REFERENCES SUMMARIZED:

Health technology assessments
No literature identified.

Systematic reviews and meta-analyses


Randomized controlled trials


Controlled clinical trials
No information identified.

PREPARED BY:
Kristen Moulton, BA, Research Assistant
Sarah Ndegwa, BScPharm, Research Officer
Monika Mierzwinski-Urban, BA, MLIS, Information Specialist
Sarah McGill, MLIS, Information Specialist
Amanda Hodgson, MLIS, Information Specialist

Health Technology Inquiry Service
Email: [htis@cadth.ca](mailto:htis@cadth.ca)
Tel: 1-866-898-8439
APPENDIX – FURTHER INFORMATION:

Randomized controlled trials


Controlled clinical trials


Additional references