Combined continuous hormone replacement therapy: a critical review

Udoff L, Langenberg P, Adashi E Y

Authors' objectives
To evaluate the putative benefits of combined continuous hormone replacement therapy (HRT) for postmenopausal women.

Searching
MEDLINE was searched from 1981 to 1995 for English language studies. Reference lists of retrieved studies were used to locate additional articles.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and case series were included.

Specific interventions included in the review
Combined continuous and sequential hormone replacement regimens.

Participants included in the review
Postmenopausal women with intact uteri were included (n=2,909).

Outcomes assessed in the review
Vasomotor symptoms (hot flushes), uterine bleeding patterns, endometrial histology, lipid and bone density measurements and compliance with the regimen were assessed.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
Each study was assessed according to the design, number of patients enrolled, duration of study, and type and dosage of hormone used. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
A narrative review was undertaken with data presented in tables for the purpose of comparing and identifying trends. The lipid data that compared sequential and combined continuous regimens of conjugated equine oestrogen and medroxyprogesterone acetate were analysed using pooled data from 6 clinical trials.

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.
Results of the review
There were 42 studies in total: 29 RCTs and 13 case series.

The effects of both the combined continuous (decline of 14.4 mg/dL) and sequential (decline of 14.9 mg/dL) regimens produced a statistically significant treatment-associated decline in total cholesterol. The two regimens did not differ significantly in their ability to lower total cholesterol. A significant treatment-associated decrease in low-density lipoprotein cholesterol with combined continuous therapy was found (17 mg/dL) and with the sequential regimen (18.4 mg/dL). Again, no significant differences between the two regimens were found. High-density lipoprotein levels increased significantly with combined continuous HRT (1.9 mg/dL) and with the sequential regimen (3.1 mg/dL). Again, no significant differences between the two regimens were found.

Improvements were noted in vasomotor symptoms (the 13 studies examining this all found improvements post-intervention).

Uterine bleeding was found to be a common problem in the first 6 months of treatment, although there was wide variation in frequency between studies (0 - 93%). Thereafter rates of amenorrhea of 75% or greater were reported.

Most patients undergoing endometrial biopsy showed atrophic endometrium (90-100%).

Compliance with HRT was high (around 80%, but with quite a wide spread 35% - 100%).

9 studies looked at bone density and all revealed either no change or an increase in bone density over time.

Cost information
No

Authors' conclusions
Combined continuous HRT is well accepted by patients in clinical trials, effective in relieving vasomotor symptoms and produces amenorrhea, an atrophic endometrium and favourable changes in circulating lipids as well as maintaining bone density. Data on the impact of this regimen on long-term patient compliance, cardiovascular disease risk and urogenital atrophy are lacking. It is not clear whether combined continuous HRT offers advantages over sequential hormone therapy.

CRD commentary
It is unclear whether all relevant studies would have been identified through the searches used. Studies are not classified according to design; RCTs and case series are presented together and the quality of each study does not seem to have been assessed.

Bibliographic details

PubMedID
7617369

Indexing Status
Subject indexing assigned by NLM

MeSH
Bone Density; Climacteric /drug effects; Endometrium /pathology; Estrogen Replacement Therapy /adverse effects /methods; Estrogens, Conjugated (USP) /administration & dosage /adverse effects; Female; Humans; Lipoproteins
/blood; Medroxyprogesterone Acetate /administration & dosage /adverse effects; Middle Aged; Osteoporosis, Postmenopausal /prevention & control; Patient Compliance; Postmenopause

**AccessionNumber**
11995002043

**Date bibliographic record published**
28/03/1996

**Date abstract record published**
28/03/1996

**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.