Influence of oral contraceptives in the development of post-molar trophoblastic neoplasia: a systematic review

Costa H L, Doyle P

CRD summary
This review investigated the effect of oral contraceptives (OCs) compared with other methods of contraception in the development of post-molar gestational trophoblastic tumour (GTT). The authors concluded that there was no clear evidence of an association between OC use and the incidence of GTT. Although the authors’ conclusions are appropriate, they cannot be viewed as definitive given the limited evidence available.

Authors' objectives
To investigate the effect of oral contraceptives (OCs) compared with other methods of contraception on the incidence of post-molar trophoblastic neoplasia and beta-human chorionic gonadotropin (hCG) regression time.

Searching
MEDLINE, EMBASE, POPLINE, Web of Science, LILACS and the Cochrane Controlled Trials Register were searched for studies in all languages (the search end dates were not specified). The reference lists of eligible studies were checked and their authors, as well as members of the International Society for the Study of Trophoblastic Disease, were contacted for information about further studies. ISI Proceedings were also searched.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and observational studies with a comparison group and at least 6 months’ follow-up were eligible.

Specific interventions included in the review
Studies of oral estro-progestative contraceptives compared with an alternative contraceptive method or no method of contraception were eligible for inclusion. Data on progestogen-only contraceptives were excluded. The type and dose of OC was not standardised in any of the included studies.

Participants included in the review
Studies of women with gestational trophoblastic disease (GTD), defined as complete hydatidiform mole diagnosed by pathologic examination of ovular tissue and submitted to uterine evacuation, were eligible. The included studies were from developing countries as well as North America and the UK. The stage of disease in the women varied between the included studies.

Outcomes assessed in the review
Studies assessing the presence of post-molar gestational trophoblastic tumour (GTT) for which the diagnostic criteria were specified, or beta-hCG regression time (defined as the number of weeks from the uterine evacuation of GTD to regression to normal levels), were eligible. Studies stopped before the normalisation of beta-hCG were excluded. The included studies used varying definitions for GTT and in the majority of studies the criteria were broader than those recommended by the International Federation of Obstetricians and Gynaecologists (FIGO).

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed all potentially relevant studies for inclusion. Any disagreements were resolved by consensus. The authors of the primary studies were contacted when insufficient information was reported to establish eligibility.
Assessment of study quality
Studies were assessed for the adequacy of allocation concealment, randomisation, whether they used an intention-to-treat analysis, and the proportion of participants lost to follow-up in each study group. Additional information on the design and risk of confounding was collected for the observational studies (further details not provided). Two reviewers independently assessed quality and any disagreements were resolved by consensus.

Data extraction
Two reviewers independently extracted the data and any discrepancies were resolved by discussion. The risk ratio (RR) and 95% confidence interval (CI) were extracted, or calculated where the data were provided, for post-molar trophoblastic neoplasia. For one study only an adjusted odds ratio was available. Beta-hCG regression time was extracted as reported by the papers.

Methods of synthesis
How were the studies combined?
The studies were discussed in a narrative and very limited study details, primarily of the RCTs, were tabulated.

How were differences between studies investigated?
The RCTs and observational studies were considered separately.

Results of the review
Two RCTs (n=372) and 7 observational studies (2 prospective and 5 retrospective; n=1,533) were included.

Both RCTs were assessed as having adequate allocation concealment and randomisation and similar loss to follow-up in both groups. Neither used an intention-to-treat analysis and it was unclear whether they were appropriately powered to detect an effect. Five of the 7 observational studies investigated confounding factors. Detection and performance bias were potential problems in one or more of the studies.

There was no evidence of an increased risk of developing GTT in OC users compared with non-users in the 2 RCTs. One observational study provided evidence of a statistically significant increased risk of post-molar GTT with OC use compared with non-use, while another reported a statistically significant decreased risk with OC use compared with no contraceptive use and use of barrier method; there was no statistically significant difference between groups for the remaining 5 studies.

Only one observational study reported a statistically significant association between OC use and beta-hCG regression time; the remaining 3 observational studies and one RCT provided no evidence of an association.

Authors’ conclusions
There was no clear evidence of an association between oral contraceptive use during the post-molar follow-up period and the incidence of GTT.

CRD commentary
The review addressed a clear research question using defined inclusion criteria. Relevant databases were searched and unpublished and non-English language studies were sought. The review methodology was well described and included measures to avoid the introduction of error and bias. Only limited study details were provided, and there were insufficient details of the observational studies. The methodological quality of the studies was assessed and limitations were discussed. The narrative synthesis was appropriate and considered clinical and methodological heterogeneity. The authors’ conclusions are appropriate, though they cannot be viewed as definitive given the limited evidence available.

Implications of the review for practice and research
Practice: The authors stated that practitioners should no longer avoid the use of OCs in the post-molar period.

Research: The authors stated that a well-conducted RCT of very low dose OC is needed to enable definite conclusions to be drawn. GTT should be defined according to FIGO criteria.

**Bibliographic details**

Costa H L, Doyle P. Influence of oral contraceptives in the development of post-molar trophoblastic neoplasia: a systematic review. Gynecologic Oncology 2006; 100(3): 579-585

**PubMedID**

16297971

**DOI**

10.1016/j.ygyno.2005.09.031

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Chorionic Gonadotropin, beta Subunit, Human /blood; Combined Modality Therapy; Contraceptives, Oral /adverse effects; Female; Gestational Trophoblastic Disease /blood /chemically induced; Humans; Hydatidiform Mole /drug therapy /surgery; Pregnancy; Randomized Controlled Trials as Topic; Uterine Neoplasms /blood /chemically induced

**AccessionNumber**

12006001142

**Date bibliographic record published**

31/08/2007

**Date abstract record published**

31/08/2007

**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.