Hormonal contraceptive use among women with liver tumors: a systematic review

Kapp N, Curtis KM

CRD summary
The authors concluded that the use of low-dose combined oral contraceptives or progestogen-only contraceptives did not appear to influence lesion regression or progression in women with focal nodular hyperplasia (benign liver tumour). Given the poor quality of the included small studies and a number of methodological shortcomings in the review process, these findings should be interpreted with caution.

Authors' objectives
To evaluate the safety of hormonal methods of contraception in women with liver tumours, specifically in benign and malignant disease.

Searching
PubMed and the Cochrane Library databases were searched with no language restrictions, for peer-reviewed studies, from inception to July 2008; search terms were reported. Reference lists and review articles were handsearched for additional studies.

Study selection
Studies that used hormonal contraception, and reported outcomes, among women with liver tumours of any histological subtype, were eligible for inclusion. Studies where women did not continue or initiate hormonal contraception after tumour diagnosis were excluded.

Both included studies were in women with focal nodular hyperplasia (benign hepatic tumours from hepatocyte parenchyma proliferation); diagnosed was by magnetic resonance imaging, excision or biopsy. Women were exposed to either combined oral contraceptives or progestogen-only contraceptives following diagnosis. The mean age of women at diagnosis in one study was 35 years. The included studies were both case-series, one retrospective, undertaken in France.

The authors did not state how the papers were selected for the review or how many reviewers performed the selection.

Assessment of study quality
Studies were assessed for quality using the United States Preventative Services Task Force Quality Rating Criteria (USPSTF).

The authors did not state how many reviewers undertook the quality assessment.

Data extraction
The authors did not state how the data were extracted for the review or how many reviewers performed the data extraction. A single author was contacted without success for clarification of study data.

Methods of synthesis
The studies were combined in a narrative synthesis, with differences between studies discussed in the text and presented in a table.

Results of the review
Two studies were included in the review (n=211 women; only 35 women continued with oral contraception after tumour diagnosis). The quality of both studies was poor, with both having small sample sizes and one having a high loss to follow-up (37%) without reporting clinical outcomes. The median duration of follow-up was 45 months in one study, and a mean of 23 months in the other study.
In one study (n=23 women using combined oral contraceptives after tumour diagnosis), one of the two women who continued taking combined oral contraceptives had an increase in lesion size and the other had a decrease in lesion size. Among the 21 women who discontinued combined oral contraceptives, lesions increased in 14%, were unchanged in 52% and decreased in 34%.

In the other study (n=188 women using combined oral contraceptives or progesterone-only contraceptives after tumour diagnosis), 26 women continued with oral contraceptives. None of the seven women who continued with progesterone-only contraceptives had changes in lesion diameter or number. Of the 26 women who continued with combined oral contraceptives, one had lesion resolution and none had an increase in lesion size or number.

Authors' conclusions
Limited, poor-quality evidence suggested that for women with focal nodular hyperplasia of the liver, use of low-dose combined oral contraceptives or progestogen-only contraceptives did not appear to influence either liver lesion resolution or progression.

CRD commentary
The review question was clear but was supported by brief, but reproducible, inclusion criteria. The authors searched two databases with no language restrictions, but did not undertake a search for unpublished studies; this may have led to the exclusion of some relevant studies. The risk of reviewer error and bias was unclear, as the authors did not report their methods.

Appropriate methods to assess study quality were undertaken, but (as acknowledged by the authors) the included studies were small and of poor quality and had methodological weaknesses that could impact on the reliability of their results. Appropriate methods of synthesis were employed.

Given the poor quality of the included small studies and a number of methodological shortcomings within the review process, these findings should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.
Research: The authors stated that further research should investigate the use of hormonal contraceptives in women with malignant liver tumours.

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