Systematic review of case-control studies: oral contraceptives show no effect on melanoma risk

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Authors’ objectives
To elucidate the role of oral contraceptives in the development of malignant melanoma (MM).

Searching
MEDLINE and Cancerlit were searched, as well as references of previously collected studies. The dates of the search, and the search terms used, were not provided.

Study selection
Study designs of evaluations included in the review
Case-control studies were eligible for inclusion. The restriction to case-control studies was due to the fact that only two cohort studies, both with few MM cases, addressed this issue.

Specific interventions included in the review
Oral contraceptives. The type of oral contraception taken was not stated.

Participants included in the review
Women (no further details were given).

Outcomes assessed in the review
The incidence of MM was 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
The authors do not state that they assessed validity.

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.

A standardised questionnaire was used to abstract information on issues of study design, analysis and results, from the publications.

Study-specific crude odds ratios (ORs) and confidence intervals (CIs) were recalculated.

Methods of synthesis
How were the studies combined?
A summary OR was calculated using both fixed-effect and random-effects models. Analyses were first performed for all studies combined, then for subgroups defined by design characteristics.

How were differences between studies investigated?
A test for heterogeneity was performed, but the type of test used was not stated.
Subgroup analyses was performed on the following: year of publication; type of case group; origin of the control group; and type of exposure.

**Results of the review**

Eighteen studies, comprising 3,796 cases and 9,442 controls, were included in the review.

There was no evidence of significant heterogeneity (p=0.38). Study-specific ORs ranged from 0.13 to 1.85; however, the majority of the studies (14 out of 18) yielded ORs between 0.82 and 1.15.

The summary OR was 0.95 (95% CI: 0.87, 1.04) for the fixed-effect model and 0.95 (95% CI: 0.87, 1.05) for the random-effects model. The CIs for the ORs were nearly identical, and pointed to the absence of any effect of oral contraceptives on the risk of MM.

Oral contraceptive use did not show a significant effect on MM risk in the following subgroups: year of publication; type of case group; origin of the control group; and type of exposure.

**Authors’ conclusions**

This systematic review revealed no evidence of an effect of oral contraceptives on the risk of MM. If there is some effect of oral contraceptive use, it has to be hidden in a more complex causal structure, e.g. as an interacting factor with other exposures.

**CRD commentary**

This review focused on a good review question. The primary studies were combined appropriately.

Only two databases were searched for relevant articles, and the dates of the search and the search terms used were not provided. No attempt was made to search for unpublished literature, and thus publication bias cannot be ruled out. The inclusion and exclusion criteria were not reported, and the validity of the included studies was not assessed. Some details of the primary studies were given, but a lot of important information was missing: for instance, the types of oral contraception the participants were taking were not reported, nor was the follow-up time. This information is required in order to interpret the results. The age of the participants and the drop-out rates would also have been useful.

The authors’ conclusions follow from the results, but should be interpreted with caution given the limitations highlighted, in particular the lack of information about the type of oral contraception taken and the follow-up time.

**Implications of the review for practice and research**

In the authors’ opinion, there is no need for further direct investigations of the association between oral contraceptives and MM.

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