Progestogen-only contraceptives and the risk of stroke: a meta-analysis

CRD summary
This review of observational studies concluded that there was no increased risk of stroke for women who took progestogen-only contraceptives, but further research was needed. The review was limited by a lack of a formal quality assessment, but the authors conclusions were suitably cautious and appear reliable.

Authors' objectives
To examine the relationship between use of progestogen-only contraceptives and risk of stroke.

Searching
MEDLINE and EMBASE were searched for studies published since the early 1960s. Search terms were reported. References were screened to locate additional studies.

Study selection
Cohort or case-control studies that controlled for age and that evaluated progestogen-only contraceptives (POC) with clearly defined contraceptive users and never and past users, and that reported on the incidence of any type of stroke (ischaemic and haemorrhagic) were eligible for inclusion. Studies of hormone replacement therapy were excluded.

The included studies were all case-control studies conducted between 1989 and 1998 of women aged between 15 and 44. Most studies evaluated oral POC; one was oral and injectable and one was of Norplant. POC users were defined as taking POC at the time of the event or within one to three months before. Controls were either population, hospital or both. All studies adjusted for age in addition to one or more of smoking, education, alcohol consumption, migraine, high blood pressure and marital status. Studies defined stroke as any type or ischaemic only.

Studies were selected by two reviewers.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The numbers of cases and controls, adjusted odds ratios (OR) and 95% confidence intervals (CI) were extracted from each study. The 95% CIs were used to estimate the standard error (SE). Non-users were taken to be the reference category in all studies except one, which used never-users.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Results were combined using both fixed-effect and random-effects meta-analysis weighted by the inverse variance. Heterogeneity was assessed using Cochrane’s Q test. Publication bias was assessed with a funnel plot and a linear regression test of asymmetry.

Results of the review
Six case-control studies were included (number of cases ranged from 26 to 1,828, controls from 224 to 5,334).

There was no evidence of a difference in the risk of stroke between oral POC users and non-users OR 1.00 (95% CI 0.68 to 1.49, heterogeneity p=0.98). Similar results were seen for all routes of administration combined (OR 0.96, 95% CI 0.70 to 1.31). There was no evidence of publication bias.
Authors' conclusions
Results from observational studies showed no increased risk of stroke with POC use, but these were based on limited data and further research was needed in women with risk factors for stroke.

CRD commentary
This review specified the study inclusion criteria for study design, intervention and outcomes. The literature search did not include attempts to locate unpublished studies and it was unclear whether there were any language restrictions, so it was possible that some studies were missed. Studies were selected by two reviewers; it was not reported whether data extraction was performed in the same way. The meta-analysis was performed using appropriate statistical methods. There was no formal assessment of study quality and although the authors highlighted the limitations in their discussion, a more thorough consideration of the quality of each study would have been helpful. The authors conclusions were suitably cautious based on the limited observational evidence available and appear to be reliable.

Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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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.