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[Intervention Review]

Fertility and early pregnancy outcomes after conservative treatment for cervical intraepithelial neoplasia

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ABSTRACT

Background

Cervical intra-epithelial neoplasia (CIN) typically occurs in young women of reproductive age. Although several studies have reported the impact that cervical conservative treatment may have on obstetric outcomes, there is much less evidence for fertility and early pregnancy outcomes.

Objectives

To assess the effect of cervical treatment for CIN (excisional or ablative) on fertility and early pregnancy outcomes.

Search methods

We searched in January 2015 the following databases: the Cochrane Gynaecological Cancer Specialised Register, Cochrane Central Register of Controlled Trials (CENTRAL; *The Cochrane Library*, Issue 12, 2014), MEDLINE (up to November week 3, 2014) and EMBASE (up to week 52, 2014).

Selection criteria

We included all studies reporting on fertility and early pregnancy outcomes (less than 24 weeks of gestation) in women with a history of CIN treatment (excisional or ablative) as compared to women that had not received treatment.

Data collection and analysis

Studies were classified according to the treatment method used and the fertility or early pregnancy endpoint. Pooled risk ratios (RR) and 95% confidence intervals (CI) were calculated using a random-effects model and inter-study heterogeneity was assessed with I^2 . Two review authors (MK, AM) independently assessed the eligibility of retrieved papers and risk of bias. The two review authors then compared their results and any disagreements were resolved by discussion. If still unresolved, a third review author (MA) was involved until consensus was reached.

Main results

Fifteen studies (2,223,592 participants - 25,008 treated and 2,198,584 untreated) that fulfilled the inclusion criteria for this review were identified from the literature search. The meta-analysis demonstrated that treatment for CIN did not adversely affect the chances of conception. The overall pregnancy rate was higher for treated (43%) versus untreated women (38%; RR 1.29, 95% CI 1.02 to 1.64; 4 studies, 38,050 participants, very low quality), although the inter-study heterogeneity was considerable ($P < 0.01$). The pregnancy rates in treated and untreated women with an intention to conceive (88% versus 95%, RR 0.93, 95% CI 0.80 to 1.08; 2 studies, 70 participants, very low quality) and the number of women requiring more than 12 months to conceive (14% versus 9%, RR 1.45, 95% CI 0.89 to 2.37; 3 studies, 1348 participants, very low quality) were no different. Although the total miscarriage rate (4.6% versus 2.8%, RR 1.04, 95% CI 0.90 to 1.21; 10 studies, 39,504 participants, low quality) and first trimester miscarriage rate (9.8% versus 8.4%, RR 1.16, 95% CI 0.80 to 1.69, 4 studies, 1103 participants, low quality) was similar for treated and untreated women, CIN treatment was associated with an increased risk of second trimester miscarriage, (1.6% versus 0.4%, RR 2.60, 95% CI 1.45 to 4.67; 8 studies, 2,182,268 participants, low quality). The number of ectopic pregnancies (1.6% versus 0.8%, RR 1.89, 95% CI 1.50 to 2.39; 6 studies, 38,193 participants, low quality) and terminations (12.2% versus 7.4%, RR 1.71, 95% CI 1.31 to 2.22; 7 studies, 38,208 participants, low quality) were also higher in treated women.

The results should be interpreted with caution. The included studies were often small with heterogenous design. Most of these studies were retrospective and of low or very low quality (GRADE assessment) and were therefore prone to bias. Subgroup analyses for the individual treatment methods and comparison groups and analysis to stratify for the cone length was not possible.

Authors' conclusions

This meta-analysis suggests that treatment for CIN does not adversely affect fertility, although treatment was associated with an increased risk of miscarriage in the second trimester. These results should be interpreted with caution as the included studies were non-randomised and many were of low or very low quality and therefore at high risk of bias. Research should explore mechanisms that may explain the increase in mid-trimester miscarriage risk and stratify this impact of treatment by the length of the cone and the treatment method used.

PLAIN LANGUAGE SUMMARY

Fertility and early pregnancy outcomes after treatment for cervical pre-cancer (cervical intra-epithelial neoplasia)

The issue

Preterm birth risk is higher after local treatment for precancer of the neck of the womb (cervix), yet there are only a few research studies that have investigated the effect on fertility and early pregnancy outcomes following treatment.

The aim of the review

We aimed to assess whether treatment for this cancer - cervical intra-epithelial neoplasia (CIN) - adversely affects the chances of a successful conception and pregnancy outcomes in the first and second trimesters (less than 24 weeks of gestation).

What are the main findings?

We included all studies that assessed fertility and early pregnancy outcomes in women who had local treatment of CIN versus untreated women. We identified fifteen suitable studies.

Fertility outcomes

The results suggest that local treatment of the cervix does not adversely affect the ability to conceive; in fact the overall pregnancy rate was higher for treated women when compared to untreated women (43% versus 38%). There was no difference in the pregnancy rates in women that intended to conceive (88% treated versus 95% untreated) or in the number of women requiring more than 12 months to conceive (15% treated versus 9% untreated).

Early pregnancy outcomes

The rates of total (less than 24 weeks of gestation) and first trimester (less than 12 weeks of gestation) miscarriage were no different. However, women after treatment had a significantly higher second trimester miscarriage rate (between 12 and 24 weeks of gestation) compared to untreated controls (1.6% versus 0.4%). The rates of ectopic pregnancies and terminations of pregnancy were higher for treated versus untreated women.

What is the quality of the evidence?

The results should be interpreted with caution as the included studies were small and of mixed design. Most of the studies were of low quality and retrospective (looking at information recorded previously). Investigation of the effect of different treatments techniques and of the size of the tissue removed (i.e. cone length) was not possible.

What are the conclusions?

The results suggest that treatment for CIN does not adversely affect the chances of a successful conception, although treatment is associated with an increased risk of miscarriage in the second trimester. These conclusions should be interpreted with caution as the quality of the included studies was low or very low. Future research should investigate the impact related to the extent of the treatment and the treatment method used.