# Targeted Update

## GnRH agonists for women with endometrioma prior to assisted reproductive technology

This is a Targeted update of one of the comparisons of the Cochrane Review

Benschop L, Farquhar C, van der Poel N. Interventions for women with endometrioma prior to assisted reproductive technology. Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.: CD008571. DOI: 10.1002/14651858.CD008571.pub2.

Latest search was performed:  23 February 2015

Results of the search, list of new references, details of updates to methods, study characteristics, risk of bias assessments and details of data analyses can be found in Supplementary material.

This Targeted update document was prepared by Hanna Bergman[1], Dennis T Kahn[1], and Karla Soares-Weiser[2]. Data were taken from the previously published full review and from results of the updating process carried out by Hanna Bergman[1], Dennis T Kahn[1], and Artemisia Kakourou[1]. The abstract was adapted from the previously published full review.

## What's a Targeted Update?

Targeted Updates are two to three-page documents that use the Cochrane Review as their foundation, but focus on updating only one or two important comparisons, and the seven most relevant outcomes. They include an updated Summary of Findings table and Abstract, and use Cochrane methodology. The full search results, risk of bias assessments, analyses, and references do not form part of the Targeted Update, but are available as supplementary information. Targeted Updates are intended for use by policy makers.

## What's the context for this Targeted Update?

The topic for this Targeted Update was identified by the Cochrane Gynaecology and Fertility Group editorial base as being in need of an update.

## What's new?

This Targeted Update identified two new studies for GnRH agonists compared to expectant management. There is a lack of evidence and further RCTs are required, especially for those measuring live birth and adverse outcomes.

Up-to-date as of February 2015.

The Targeted Update 'Surgery for women with endometrioma prior to assisted reproductive technology' covers another treatment from the same Cochrane review.

There is a lack of evidence for live birth; no studies reported on this outcome. There was no evidence of benefit with any of the interventions in the review. Further research on the best approach for women with endometrioma prior to ART needs to be a priority.

## Background
Endometrioma is a cyst of endometriosis in the ovaries. As assisted reproductive technology (ART) cycles involve oocyte pickup from the ovaries, an endometrioma may interfere with the outcome of ART.

## Objectives
To determine the effectiveness and safety of gonadotropin-releasing hormone (GnRH) agonists for improving reproductive outcomes among women with endometrioma, prior to undergoing ART cycles.

## Search methods
Cochrane Menstrual Disorders and Subfertility Group Specialised Register of trials, CENTRAL (The Cochrane Library), EMBASE, MEDLINE, CINAHL, trial registers for ongoing and registered trials (February 2015), and trials registers (ClinicalTrials.gov and WHO ICTRP) for ongoing and registered trials (April 2015) were searched.

## Selection criteria
Randomised controlled trials (RCTs) of GnRH agonists versus expectant management for endometrioma prior to ART were included. The primary outcomes were live birth and adverse outcomes (such as miscarriage, ectopic pregnancy, multiple pregnancies, ovarian hyperstimulation syndrome (OHSS), or ovum pick up pain or infection).

## Data collection and analysis
The trials were independently identified and assessed for risk of bias by two reviewers. Outcomes were expressed as Peto odds ratios (OR) with 95% confidence intervals (CI).

## Main results
Two new trials with 143 participants were identified and included in this Targeted Update. In addition, one ongoing study was found. No trials were included in the original review for this comparison.

The two studies stated that the women had endometriosis but did not explicitly state how many women had endometrioma. Despite this lack of clarity, these studies were included since the study results apply to milder forms of endometriosis.

The two included trials were adequately randomised. However, in one of the studies only participants who completed the study were analysed. Whether allocation was concealed was unclear in both studies. There was a high risk of reporting bias, as both studies failed to report on the primary outcome live birth. The studies were not blinded, but outcomes are not likely to be affected by performance or detection bias.

The evidence on OHSS following GnRH agonist treatment compared with expectant management was of very low quality, and estimates are imprecise (OR 0.50, 95% CI 0.10 to 2.56). No trials reported on other adverse outcomes.

Similarly, the evidence on clinical pregnancy with GnRH agonists when compared with expectant management was of very low quality and estimates are imprecise (OR 1.14, 95% CI 0.56 to 2.32).

## Implications and conclusions
There is a lack of evidence on live birth with GnRH agonists as compared with expectant management for women with endometrioma prior to ART. The evidence on OHSS and clinical pregnancy following GnRH agonists compared with expectant management was downgraded due to design (unclear allocation concealment, incomplete analysis and reporting, and a lack of blinding) and imprecision (few, small studies, wide confidence intervals) and consequently, the evidence was considered to be of very low certainty and estimates are imprecise. Further RCTs of GnRH agonists for women with endometrioma undergoing ART are required, especially studies measuring live birth rate and adverse outcomes.

# Summary of Findings: GnRH agonists for women with endometrioma prior to assisted reproductive technology

*Patients and setting*: Women with endometrioma undergoing assisted reproductive technology. Studies were set in Greece and the USA.

*Comparison:* Pre-treatment GnRH agonists versus expectant management.

| Outcome | Plain language summary | Absolute effect | | Relative effect (95% CI) Nº of participants & studies | Certainty of the evidence (GRADE) |
|---|---|---|---|---|---|
| | | Expectant management | GnRH agonist | | |
| Live birth | No studies reported on this outcome. | | | | |
| Ovarian Hyperstimulation Syndrome (OHSS) | The evidence on OHSS following GnRH agonist treatment compared with expectant management was of very low quality and estimates are imprecise. | 67 per 1000 | 34 per 1000 | OR 0.50 (0.10 to 2.56) Based on data from 120 participants in 1 study | ⊕OOO VERY LOW[1,2,3] |
| | | Difference 33 fewer per 1000 (95% CI from 60 fewer to 88 more) | | | |
| Clinical pregnancy | The evidence on clinical pregnancy with GnRH agonists when compared with expectant management was of very low quality and estimates are imprecise | 315 per 1000 | 344 per 1000 | OR 1.14 (0.56 to 2.32) Based on data from 143 participants in 2 studies | ⊕OOO VERY LOW[3,4,5] |
| | | Difference 29 more per 1000 (95% CI from 110 fewer to 201 more) | | | |

CI= confidence interval; GnRH=gonadotropin-releasing hormone; OR=Odds ratio

[1] Design (-1): Method of allocation concealment was unclear, and only completers were analysed (attrition bias). The study was not blinded, but the outcome is not likely to be affected by performance and detection bias.

[2] Imprecision (-2): One small study and the 95% CIs around the pooled estimate of effect include both appreciable benefit and appreciable harm, as well as no effect.

[3] Indirectness (-1): Unclear whether the participants in the study had endometrioma or endometriosis.

[4] Design (-1): Method of allocation concealment was unclear. The study was not blinded, but the outcome is not likely to be affected by performance and detection bias.

[5] Imprecision (-2): Two small studies and the 95% CI around the pooled estimate of effect includes both appreciable benefit and appreciable harm, as well as no effect.