GnRH agonist therapy as ovarian protectants in female patients undergoing chemotherapy: a review of the clinical data

Beck-Fruchter R, Weiss A, Shalev E

CRD summary
This review assessed the evidence for use of GnRH agonist therapy as a gonadoprotectant for women who received chemotherapy and concluded that there was insufficient evidence to support its effectiveness. In light of multiple methodological shortcomings and poor reporting, the authors’ conclusions should be interpreted with caution.

Authors’ objectives
To assess the evidence for the use of gonadotropin-releasing hormone agonist (GnRH) therapy as a gonadoprotectant for women receiving chemotherapy.

Searching
MEDLINE was searched without language restrictions from 1966 to February 2008 for published peer-reviewed articles; only English-language studies were included. Search terms were reported. Reference lists of included articles were searched for additional studies.

Study selection
Studies in which ovarian function was reported on following the administration of GnRH agonists with chemotherapy were eligible for inclusion. Excluded studies combined a GnRH antagonist and agonist or did not separate between patients who received GnRH agonist and those who did not receive the agonist. GnRH agonists used in included studies comprised: buserelin; leuprolide acetate; triptorelin; triptorelin acetate; goserelin; and goserelin acetate. Diseases among participants included Hodgkin's lymphoma, non-Hodgkin's lymphoma, systemic lupus erythematosus, breast cancer and haematological oncologic pathology. Included studies used ovarian function tests as a surrogate end point for fertility. Reported outcomes for included studies comprised menstruation, cycle regularity, hormone levels, pregnancy and ovarian sonography. Mean or median age of participants ranged from 16.8 to 43 years.

The authors stated neither how papers were selected for review nor how many reviewers performed the selection.

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

Data extraction
For each study, data for preserved ovarian function and premature ovarian failure or persistent amenorrhea were extracted as percentages.

The authors stated neither how data were extracted for review nor how many reviewers performed the data extraction.

Methods of synthesis
Overall percentages of women with preserved ovarian function or premature ovarian failure were calculated for all studies. The statistical significance of between-group differences was assessed using Fisher's exact test.

Results of the review
A total of 12 studies were included in the review (n=690, range five to 157): data on ovarian function were obtained for 579 women, 345 of whom received GnRH. Two studies were randomised controlled trials (n=47) and 10 were case-series (three without controls). Where reported, duration of follow-up ranged from less than one to eight years.

The proportion of preserved ovarian function was greater (91% versus 41%) and rates of premature ovarian failure or persistent amenorrhea were lower (9% versus 59%) in the study group compared with the control group. In the
randomised studies (two studies) regular menstruation was resumed in 82% of the study group compared with 46% in the control group.

Authors’ conclusions
There was insufficient evidence to illustrate that GnRH agonist cotreatment was effective for the protection of the ovary from chemotherapy damage.

CRD commentary
The review question was clear and included broad (but potentially reproducible) inclusion criteria. The limited literature search was restricted to publications in English and unpublished studies were not sought; therefore, language bias could have been present and some studies may have been missed. The methods used for study selection and data extraction were not reported, so it was unclear whether methods were used to minimise error and bias. No formal assessment of study quality was reported, which made it difficult to assess the reliability of the included data. Most studies were small and contained less than 60 participants. Some studies did not have a control group. Given the heterogeneity across studies, the decision to employ a limited statistical synthesis may not have been appropriate. In light of the shortcomings highlighted for the review process, lack of assessment of study quality, heterogeneity across study outcomes, paucity of experimental studies and small sample sizes, the authors conclusions 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 a large randomised controlled trial with adequate follow-up was required to assess GnRH agonists for fertility preservation in young women who received chemotherapy.

Funding
Not stated.

Bibliographic details

PubMedID
18820006

DOI
10.1093/humupd/dmn041

Original Paper URL
http://humupd.oxfordjournals.org/cgi/content/abstract/14/6/553

Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Adult; Antineoplastic Agents /adverse effects; Case-Control Studies; Female; Gonadotropin-Releasing Hormone /agonists /therapeutic use; Humans; Infertility, Female /chemically induced /prevention & control; Middle Aged; Ovary /drug effects /physiology; Protective Agents /therapeutic use; Randomized Controlled Trials as Topic; Treatment Outcome

AccessionNumber
12009101248
Record Status
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.