Ovulation induction drug therapy for anovulatory infertility associated with polycystic ovary syndrome

Corabian P, Scott A

Record Status
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Citation

Authors' objectives
This report is a systematic review and critical appraisal of the evidence on the use of ovulation induction (OI) drug therapy to manage anovulatory infertility associated with polycystic ovary syndrome (PCOS) in women of reproductive age. The aim was to provide the current published scientific evidence about its safety and efficacy/effectiveness in terms of pregnancy rate in this category of infertile patients in response to a request for information from Alberta Health and Wellness.

Authors' conclusions
Ovulation induction using drugs (OI drug therapy) is the most performed therapy in reproductive-aged women with anovulatory infertility. Anovulatory infertility is associated with polycystic ovary syndrome (PCOS) in the majority of cases and it appears to be difficult to manage safely and successfully with OI drug therapy in this population. The reviewed evidence was obtained from randomized controlled studies of small to moderate sample size, short duration, and limited methodology. The investigators used different approaches, treatment protocols, study population, definitions of outcome measures and types of outcomes. The question on which is the safest and the most effective OI drug therapy in these women does not have a clear answer yet. According to the available evidence: - CC therapy remains the first choice of OI drug therapy because of its relative safety, effectiveness in achieving ovulation, simple mode of administration and relatively low cost. However, success in achieving ovulation equates with success in achieving pregnancy in only half of cases. The increased risk of multiple pregnancies associated with the use of CC should also be considered. - In women who do not ovulate or do not conceive in response to CC therapy, gonadotrophin therapy is the next medication of choice. It is still not certain whether any type of gonadotrophin preparations currently available is superior in terms of improving pregnancy rates and reducing complication rates. Low-dose gonadotrophin regimens (regardless of preparations used) may be considered in order to reduce the incidence of multiple follicle developments and the associated complications. - Metformin as a pre-treatment and co-treatment with CC seems successful in increasing chances of achieving pregnancy in selected cases and has been proposed as a sequential treatment before the use of gonadotrophins. However, data regarding its use alone or as an adjunct to CC remain to be confirmed before recommending it as a standard therapy. - The clinical utility of using pulsatile gonadotrophin releasing hormone (GnRH) therapy for this indication remains to be established. - There is no clinical advantage in the routine use of GnRH analogue in addition to gonadotrophin therapy for this indication. - The role of using other adjuncts in addition to CC therapy or to gonadotrophin therapy for this indication has yet to be firmly established. OI drug therapy using gonadotrophins should be restricted to centers with the expertise and the equipment necessary to make appropriate clinical decision relating to the treatment and management of the associated complications. Women with PCOS considering OI drug therapy to manage their anovulatory infertility should be aware that: regardless of the approach used, they appear to be at increased risk for multifollicular development and spontaneous abortion; - the risk of developing serious complications such as multiple pregnancies and ovarian hyperstimulation syndrome appears to be higher when gonadotrophin therapy is used; and - there may be a reduced probability of a male live birth following CC therapy. Large scale RCTs, well-designed and conducted, on the use of various approaches to OI drug therapy for longer time are needed to provide definitive evidence on their value in managing anovulatory infertility associated with PCOS. An accurate and detailed sub-classification of women with PCOS may have important implications in the search for the safest and most effective OI drug therapy for this indication. Data on the overall cost of using various approaches to OI drug therapy are needed to aid in the couples decision-making and to assist in the formulation of
policy for using this therapy to manage this indication.

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**Address for correspondence**
1200, 10405 Jasper Avenue, Edmonton, Alberta, Canada, T5J 3N4. Tel: +1 780 448 4881; Fax: +1 780 448 0018
Email: djuzwishin@ihe.ca

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