Superovulation and intrauterine insemination were most effective for infertility


Question
In couples with unexplained infertility or in whom the woman has minimal endometriosis, are induction of superovulation with gonadotropins and intrauterine insemination (IUI) effective for achieving pregnancy?

Design
Randomised, single-blind, controlled trial with a mean follow-up of 5 menstrual cycles.

Setting
10 clinical sites in the United States.

Patients
932 couples who had been infertile for >1 year, who had negative results on serum antisperm antibody testing, of whom the women were <40 years of age (mean age 35 y), and of whom the men were <55 years of age (mean age 35 y). Women had a normal uterine cavity (or had been treated for minimal or mild endometriosis ≥6 months before trial entry), in-phase endometrium, patent tubes, menstrual cycle lengths of 24 to 40 days, and normal serum follicle-stimulating hormone (FSH) and thyrotropin levels on days 1 to 5 of a menstrual cycle. Men had motile sperm. Exclusion criteria included previous use of in vitro fertilisation or other assisted reproductive technology; history of chronic disease, chemotherapy, radiation to the abdomen or pelvis, or tubal surgery; or extensive tubal adhesions. Follow-up was 82%.

Intervention
Couples were allocated to 1 of 4 groups: IUI (n = 234), superovulation induced by FSH plus intracervical insemination (ICI) (n = 234), superovulation and IUI (n = 231), or ICI (control, n = 233). ICI and IUI were timed to the increase in urinary luteinising hormone excretion. FSH, 150 IU intramuscularly, was given daily in the superovulation groups until ≥2 follicles reached an average size of ≥18 mm.

Main outcome measure
Pregnancy rate per couple.

Main results
Superovulation plus IUI (P < 0.001), superovulation and ICI (P = 0.006), and IUI (P = 0.01) resulted in more pregnancies than did ICI alone (Table). Superovulation with IUI was most effective.

Conclusion
In couples with unexplained infertility, superovulation with intrauterine insemination was more efficacious for increasing the pregnancy rate than was intrauterine insemination alone or superovulation with intracervical insemination. Sources of funding: In part, National Institute of Child Health and Human Development and Serono Laboratories. Ovulation-detection kits supplied by Quidel.

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Pregnancy rates per couple after ≤4 infertility treatment cycles of infertility treatment vs intracervical insemination (ICI) for unexplained infertility*

<table>
<thead>
<tr>
<th>Comparisons</th>
<th>Treatment</th>
<th>Control</th>
<th>RBI (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUI vs ICI</td>
<td>18%</td>
<td>10%</td>
<td>82% (14 to 92)</td>
<td>13 (7 to 33)</td>
</tr>
<tr>
<td>Superovulation and ICI vs ICI</td>
<td>19%</td>
<td>10%</td>
<td>90% (20 to 205)</td>
<td>12 (7 to 39)</td>
</tr>
<tr>
<td>Superovulation and IUI vs ICI</td>
<td>33%</td>
<td>10%</td>
<td>238% (122 to 419)</td>
<td>5 (4 to 7)</td>
</tr>
</tbody>
</table>

*IUI = intrauterine insemination. Other abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.

Commentary
Treatment of unexplained infertility of relatively short duration is often a challenge for physicians who manage reproductive problems. Failure to achieve a pregnancy after 1 year of trying leads to emotional distress for patients and substantial demand on physicians for a quick fix.

This large controlled study by Guzick and colleagues is helpful in showing the efficacy of superovulation with IUI for unexplained infertility and shows its superiority in achieving pregnancy over IUI or superovulation alone, even with sperm of dubious quality. However, the control group of timed ICI for ≤4 menstrual cycles may not be an appropriate comparative “no-treatment” arm, as intercourse generally occurs more than once per cycle and couples usually will continue to try for ≥4 cycles. When a couple is young, the infertility period has been relatively short (<36 mo), and no major male or female reproductive problems have been diagnosed, spontaneous conception leading to live births, not merely pregnancy, is a real and likely outcome (1). The cost of the IUI and superovulation procedure in time, drug use, and personal invasion must be considered. Using this regimen, concerns exist about hyperstimulation syndrome (6 women were hospitalised) and the substantial rate of multiple pregnancy (20% overall and 6% for triplets and quadruplets) with its attendant costs and risks for prematurity and handicap (2).

The study emphasises the need for patients being offered this type of treatment to be well counselled and for treatment to be undertaken only within reproductive medicine units capable of dealing with the inevitable complications.

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References