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Efficacy of monotherapy letrozole versus methotrexate for the management of ectopic pregnancy: a systematic review and meta-analysis of comparative studies

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Ectopic pregnancy (EP) is a serious condition often treated with methotrexate. Letrozole, a safer aromatase inhibitor, may offer an effective alternative. This study presents a meta-analysis comparing the efficacy and safety of single-agent letrozole versus methotrexate for EP management.

Study type

Systematic review and meta-analysis of 6 studies
(3 randomized controlled trials + 3 prospective cohorts)

Patients

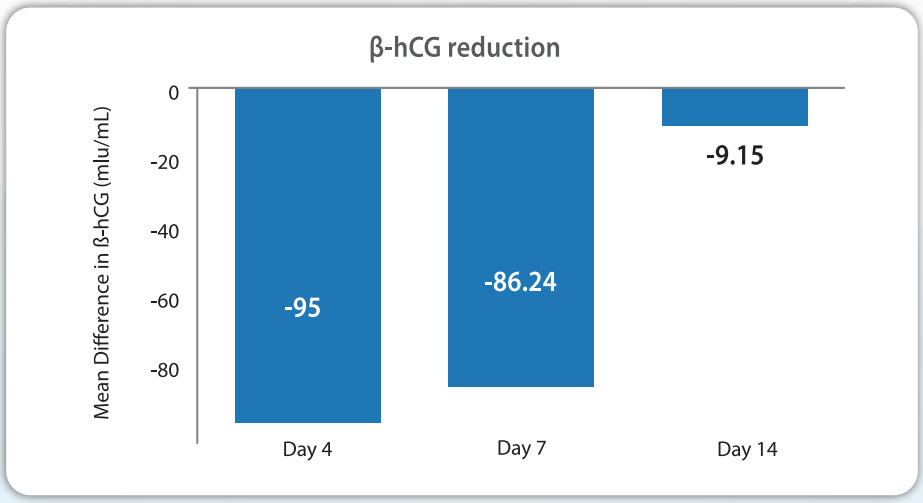
260 patients

Intervention

- Letrozole | N=130
- Methotrexate | N=130

Results

- Treatment success rates were comparable between groups (RR = 1.05; 95% CI: [0.94, 1.17]; p = 0.40). The pooled analysis showed no heterogeneity (I^2 = 0%, p = 0.58)
- Letrozole was associated with significantly lower β-hCG levels.



Mechanism of action

Methotrexate

Inhibits the formation of tetrahydrofolate

↓

Inhibits DNA synthesis

↓

Trophoblastic regression

Limitations

- Systemic toxicity
- Multiple contraindications
- Need for intensive monitoring

Letrozole

Aromatase inhibition

↓

Inhibits estrogen, progesterone, VEGF

↓

Trophoblastic regression

Advantages

- More targeted hormonal mechanism
- Better safety and tolerability
- Less monitoring burden.

Safety Letrozole showed a better safety profile with higher platelet counts and lower liver enzymes. AMH levels were similar between groups.

Conclusions Letrozole may be a promising alternative to methotrexate for the medical management of EP. This meta-analysis indicates that letrozole provides comparable efficacy to methotrexate while offering a better safety profile, highlighting its potential as a safer treatment option.

Ref: Abu-Zaid A, Alsabban M, Nazer A, Alabdrabalamir S, Jamjoom MZ, Alqarni SMS, Albelwi H, Baradwan S, Ebeid SM, Abuzaid M, et al. Efficacy of Monotherapy Letrozole Versus Methotrexate for the Management of Ectopic Pregnancy: A Systematic Review and Meta-Analysis of Comparative Studies. Journal of Clinical Medicine. 2025; 14(18):6523. https://doi.org/10.3390/jcm14186523

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