Cochrane Review Summaries—July 2020

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Abstract

This feature highlights recently published Cochrane Reviews of interest to the readers of *Obstetrics & Gynecology*. The brief summaries are published below, and the complete references, along with a hyperlink, are listed in Box 1.

Box 1. Abstracts Discussed in This Summary

1. Dodd JM, Grivell RM, O'Brien CM, Dowswell T, Deussen AR. Prenatal administration of progestogens for preventing spontaneous preterm birth in women with a multiple pregnancy. The Cochrane Database of Systematic Reviews 2019, Issue 11. Art. No.: CD012024. Available at: <https://doi.org/10.1002/14651858.CD012024.pub3>.
2. Duley L, Meher S, Hunter KE, Seidler AL, Askie LM. Antiplatelet agents for preventing preeclampsia and its complications. The Cochrane Database of Systematic Reviews 2019, Issue 10. Art. No.: CD004659. Available at: <https://doi.org/10.1002/14651858.CD004659.pub3>.

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3. Wang R, Danhof NA, Tjoh-Kon-Fat RI, Eijkemans MJC, Bossuyt PMM, Mochtar MH, et al.

Interventions for unexplained infertility: a systematic review and network meta-analysis. The

Cochrane Database of Systematic Reviews 2019, Issue 9. Art. No.: CD012692. Available at:

<https://doi.org/10.1002/14651858.CD012692.pub2>.

Prenatal Administration of Progestogens for Preventing Spontaneous Preterm Birth in Women With Multiple Pregnancies

More than half of twin pregnancies result in preterm delivery (before 37 weeks of gestation). This may lead to adverse health outcomes in neonates. Progesterone has a significant role in prolonging pregnancy, possibly through suppression of uterine smooth muscle activity.¹

This systematic review included 16 trials involving 4,548 women in multiple countries. Included trials compared either intramuscular (IM) injection or vaginal administration with no treatment or placebo. The risk of bias was low for the majority of the included studies. More women given IM progesterone delivered at less than 34 weeks of gestation when compared with those given placebo (risk ratio [RR] 1.54, 95% CI 1.06–2.26; low-quality evidence). There were no clear group differences in any of the other maternal or neonatal outcomes with IM administration. There were no clear group differences in preterm birth before 34 weeks of gestation (average RR 0.90, 95% CI 0.66–1.23; low-quality evidence) or any other maternal or neonatal outcomes. Both the IM and vaginal progesterone groups had a higher incidence of prenatal death compared with placebo or no treatment (RR 1.45 and 1.23, respectively). Still, there was high heterogeneity between studies and significant uncertainty around the effects, with CIs overlapping at 1.0. Pregnant women who had vaginal progesterone had slightly fewer cesarean deliveries compared with those receiving no treatment (RR 0.92, 95% CI 0.86–0.98; n=1,919; five studies). Neonates whose mothers had vaginal progesterone were less likely to require mechanical ventilation compared with those receiving placebo or no treatment (RR 0.70, 95% CI 0.52–0.94; n=2,695;

four studies). This supports the previous recommendation by the American College of Obstetricians and Gynecologists that progesterone should not be used in women with multiple gestations to prevent preterm birth.²

Bottom Line: Giving women with multiple gestations progesterone therapy does not reduce preterm birth and may be associated with harms. However, there is uncertainty surrounding much of the evidence on the topic.

Antiplatelet Agents for Preventing Preeclampsia and its Complications

Preeclampsia occurs in about 2–10% of pregnancies worldwide, with higher incidences occurring in low-income countries. Furthermore, women who develop preeclampsia in low-income countries have higher maternal mortality rates than those in high-income areas.³

This review explored the use of antiplatelet agents to prevent preeclampsia. The authors included 77 randomized controlled trials, with more than 40,000 women at risk for developing preeclampsia. When compared with placebo or no treatment, using antiplatelet agents reduced the risk of developing preeclampsia by 18% (RR 0.82, 95% CI 0.77–0.88; high-quality evidence), with a number needed to benefit of 61. There were also reductions in other outcomes, such as preterm birth at less than 37 weeks of gestation, fetal deaths, neonatal deaths or death before hospital discharge, neonates diagnosed as small for gestational age, and pregnancies with serious adverse outcomes. Of note, this update incorporated an individual participant data analysis. The individual participant data are available from 36 trials, including 34,514 women. Individual participant data analyses allow for even more robust combining of trial data and improve the precision of subgroup analyses. This updated review concludes that the use of antiplatelet agents might be effective in preventing preeclampsia and other adverse outcomes. The optimal dose and timing to begin the therapy are less clear, but recommendations typically call for doses of 75 mg or more to begin optimally by 16 weeks of gestation.

Bottom Line: Administering low-dose antiplatelet agents to pregnant women who are at risk of developing preeclampsia reduces the development of preeclampsia by 18%. Because the list of risk factors for preeclampsia is long,⁴ health care professionals should be aware of the potential benefits of these agents.

Interventions for Unexplained Infertility: A Systematic Review and Network Meta-analysis

It is estimated that a standard fertility evaluation will fail to detect an abnormality in up to 30% of infertile couples. Current clinical guidelines from both the American Society for Reproductive Medicine and the Canadian Fertility and Andrology Society note starting with simple treatments for the management of unexplained infertility before moving on to invasive techniques (eg, ovarian stimulation, intrauterine insemination [IUI], in vitro fertilization [IVF], and intracytoplasmic sperm injection [ICSI]).^{5,6}

This systematic review used a network meta-analysis approach to evaluate the effectiveness and safety of different clinical interventions. This compares multiple treatments simultaneously by using both direct and indirect evidence rather than traditional head-to-head comparisons.

The review included 27 trials involving 4,439 couples; of these, 24 trials including 3,983 couples contributed to the network analysis. The authors conclude that there was insufficient evidence of differences in live-birth rates between expectant management (timed sexual intercourse) and the other interventions (ovarian stimulation, IUI, ovarian stimulation–IUI, and IVF–ICSI; low-certainty evidence). This suggests that, if the chance of live birth after expectant management is assumed to be 17%, the chance after ovarian stimulation, IUI, ovarian stimulation–IUI, and IVF would be 9–28%, 11–33%, 15–37%, and 14–47%, respectively. Compared with expectant management or IUI, other interventions may increase the odds of multiple pregnancy. Among three trials (725 couples) that explored the responses in couples with a “poor prognosis of natural conception,” ovarian stimulation–IUI (odds ratio 4.48, 95% CI 2.00–10.1) and IVF–ICSI (odds ratio 4.99, 95% CI 2.01–12.04) increased the live-birth rate compared

with expectant management. The authors note that about half of the studies were performed before 2000 and that recent trials had much more intensive ovarian-stimulation protocols. Additional studies using these techniques with current protocols are recommended by the authors.

Bottom Line: There is no single optimal therapy strategy for couples with unexplained infertility.

Ovulation stimulation alone or in combination with IUI may increase the chances of multiple pregnancy.

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