



Don't start Aspirin, LMWH, and/or Progesterone to maintain pregnancy in a patient with an unexplained recurrent pregnancy loss

Women with unexplained recurrent miscarriages have an excellent prognosis for future pregnancy outcomes without pharmacological intervention if offered supportive care alone in the setting of a dedicated early pregnancy assessment unit. These women can be reassured that the prognosis for a successful future pregnancy with supportive care alone is in the region of 75%.

Two recent randomized controlled trials reported that neither of these interventions improves the live birth rate among women with unexplained recurrent miscarriage. The data suggest that the use of empirical treatment in women with unexplained recurrent miscarriages is unnecessary and should be resisted.

Royal College of Obstetricians and Gynaecologists Green-top Guideline Number 17. The Investigation and Treatment of Couples with Recurrent First-trimester and Second-trimester Miscarriage. RCOG, London 2011

Coomarasamy A, Williams H, Truchanowicz E, Seed PT, Small R, Quenby S, Gupta P, Dawood F, Koot YE, Atik RB, Bloemenkamp KW, Brady R, Briley A, Cavallaro R, Cheong YC, Chu J, Eapen A, Essex H, Ewies A, Hoek A, Kaaijk EM, Koks CA, Li TC, MacLean M, Mol BW, Moore J, Parrott S, Ross JA, Sharpe L, Stewart J, Trépel D, Vaithilingam N, Farquharson RG, Kilby MD, Khalaf Y, Goddijn M, Regan L, Rai R. PROMISE: first-trimester progesterone therapy in women with a history of unexplained recurrent miscarriages - a randomised, double-blind, placebo-controlled, international multicentre trial and economic evaluation. *Health Technol Assess.* 2016 May;20(41):1-92. doi: 10.3310/hta20410. PMID: 27225013; PMCID: PMC4904188.

Coomarasamy A, Devall AJ, Cheed V, Harb H, Middleton LJ, Gallos ID, Williams H, Eapen AK, Roberts T, Ogwulu CC, Goranitis I, Daniels JP, Ahmed A, Bender-Atik R, Bhatia K, Bottomley C, Brewin J, Choudhary M, Crosfill F, Deb S, Duncan WC, Ewer A, Hinshaw K, Holland T, Izzat F, Johns J, Kriedt K, Lumsden MA, Manda P, Norman JE, Nunes N, Overton CE, Quenby S, Rao S, Ross J, Shahid A, Underwood M, Vaithilingam N, Watkins L, Wykes C, Horne A, Jurkovic D. A Randomized Trial of Progesterone in Women with Bleeding in Early Pregnancy. *N Engl J Med.* 2019 May 9;380(19):1815-1824. doi: 10.1056/NEJMoa1813730. PMID: 31067371.

In the PROMISE trial (first-trimester progesterone therapy in women with a history of unexplained recurrent miscarriages), the results show that first-trimester progesterone therapy does not appear to have clinically significant benefits in pregnant women with a history of unexplained recurrent miscarriage. The effect of progesterone in women with bleeding in early pregnancy differed according to the number of previous miscarriages, with a suggestion of benefit among women who had had three or more previous miscarriages.

In women with bleeding in early pregnancy, progesterone therapy administered during the first trimester did not result in a significantly higher incidence of live births. Moreover, in women with multiple gestations, prophylactic progesterone is ineffective in preterm labor prevention or reduction of overall twin morbidity.

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