Progesterone for Prevention of Preterm Birth – Evidence-based Indications


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Background: The prevention and treatment of preterm birth remains an unsolved problem in modern obstetrics. Progesterone has a variety of actions on the myometrium and the cervix, among others inhibition of myometrial contractility and a cervix strengthening effect by inhibiting the production of proinflammatory cytokines and prostaglandins as well as by reducing the synthesis of proteins, which play a crucial role in initiating labour. Consequently, progesterone may be a promising candidate for the prevention of preterm birth.

Material and Methods: We searched PubMed from 1956 to August 2014 using a combination of key words and text words related to preterm birth and progesterone. (‘progesterone’, progesterins, 17-OHPC). The aim of the literature search was to determine evidence-based indications for the use of progesterone in the prevention of preterm birth.

Results: (i) Patients with a singleton pregnancy and history of preterm birth should receive vaginal progesterone daily (200 mg capsule or 90 mg containing gel) from 16 + 0 to 36 + 0 weeks of gestation (alternatively 250 mg intramuscular 17-OHPC weekly): level of evidence 1a, grade of recommendation ++. Prophylactic progesterone reduces the incidence of preterm birth < 34 and < 37 weeks of gestation and perinatal mortality significantly. (ii) Patients with singleton pregnancies and a sonographically short cervix (≤ 25 mm) before 24 weeks of gestation should receive vaginal progesterone daily (200 mg capsule or 90 mg containing gel) until 36 + 6 weeks of gestation: level of evidence 1a, grade of recommendation ++. Prophylactic progesterone leads to a significant reduction in the incidence of preterm birth < 28, < 33, and < 35 weeks of gestation and is associated with a significant reduction of neonatal morbidity. (III) There is a lack of evidence to recommend vaginal progesterone or intramuscular 17-OHPC for primary tocolysis or for “adjunctive” tocolysis (in combination with conventional tocolytic agents). (IV) There is a growing body of evidence that vaginal progesterone (400 mg/day) after successful tocolysis (“maintenance therapy”) is a promising option for prolongation of pregnancy: level of evidence 1b, grade of recommendation +, (V) Data from the literature are insufficient to recommend progesterone in patients with preterm rupture of membranes or in the perioperative management of patients requiring transvaginal cervical cerclage. (VI) The vaginal administration of progesterone is well-tolerated by the patients and has only minor maternal side effects, whereas intramuscular injections of 17OHPC are associated with a significant higher rate of side effects (e.g. local pain, nausea, diarrhoea). It is mandatory to inform patients on the off label use of progesterone in pregnancy.

Discussion: Prophylactic progesterone administration is an evidence-based method for the prevention of preterm birth in women with a previous preterm birth and in pregnant women with a sonographically short cervix (≤ 25 mm) before 24 weeks of gestation. Vaginal progesterone is favoured over intramuscularly applied 17-OHPC, especially because of the lower rate of maternal side effects. Whether progesterone is an effective approach for the treatment of preterm birth as a tocolytic agent (primary, adjunctive) or for maintenance therapy after arrest of preterm labour has to be shown in further well-designed randomised and controlled trials with adequate statistical power.