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Progesterone treatment in patients undergoing cervical cerclage: a meta-analysis

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Objective

Both progesterone (Pg) and cervical cerclage (Cx) are potentially effective treatments preventing spontaneous preterm birth (SPTB). However, additional benefit of Pg treatment in women with Cx on the risk of SPTB and perinatal outcomes is unclear. The aim of this study is to evaluate the risk of SPTB in singleton pregnancies with Cx for different indications, with or without Pg treatment.

Methods

A systematic search of the literature of the last 30 years screened 322 results and assessed 43 cohort and case-control studies, including nine in our analyses with a total of 2878 patients. Additional data were obtained contacting directly corresponding authors. Studies comparing Cx alone to Cx plus Pg (Cx+Pg) were included, only if they expressed clearly indication for Cx (history of SPTB, short cervix at ultrasound (US) or abnormal physical-exam). SPTB<37 weeks was the primary outcome. Secondary core outcomes of PTB were also analyzed when possible (SPTB<34/32/28/24 weeks, P-PROM, neonatal outcomes). A meta-analysis was performed with random effect model. Heterogeneity across the studies was assessed by I2 value and the X^2-based Q-test. A P-value > 0. 10 for the Q-test or an I^2 value less than 50% revealed no obvious heterogeneity across the studies.

Results

Pooling all cases of Cx the effect of Pg was not significant [SPTB <37 Cx: 1018/2300; 44. 26 %; Cx+Pg: 222/578; 38. 41%; OR= 0. 86 (95%CI 0. 60-1. 23); p=0. 40; I2=53%]. Pooling of six studies in which Cx was performed for previous history of SPTB fail to show statistically significant effect of Pg administration [SPTB<37 Cx: 925/2116; 43. 71%; Cx+Pg: 180/484; 37. 19%; OR=0. 91 (95%CI 0. 62-1. 33); p=0. 62; I2=49%]. Pooling of two studies in which Cx was performed for short cervix at US fail to show statistically significant effect of Pg [SPTB<37 Cx: 65/138; 47. 10%; Cx+Pg: 38/74; 51. 35%; OR=1. 13 (95%CI 0. 64-2. 00); p=0. 68; I2=0%]. Pooling of two studies in which Cx was performed for abnormal physical-exam showed a statistically significant beneficial effect of Pg [SPTB<37 Cx: 28/46; 60. 86%; Cx+Pg: 4/20; 20. 00%; OR 0. 17 (95%CI 0. 05-0. 63); p=0. 008; I2=0%]. Pooling of three studies provided higher risk for SPTB<34/32 in the group of history-based Cx+Pg as compared with Cx alone [SPTB<34 Cx: 384/1789; 21. 5%; Cx+Pg: 83/289; 28. 7%; OR 1. 38 (95% CI 0. 03-1. 84); p=0. 03; I2: 0%; SPTB<32 Cx: 151/1789; 8. 4%; Cx+Pg: 45/289; 15. 6%; OR: 1. 73 (95% CI: 1. 19-2. 50); p=0. 004; I2=0%]. Other secondary outcomes and sensitivity sub-analyses did not show significant differences.

Conclusion

Pg treatment may reduce SPTB in women with Cx, when cervical length is significantly reduced. Increased risk of SPTB in Cx+Pg for first trimester history-indicated cerclage is likely due to selection bias of non-randomized studies and tendency to administer Pg in higher risk cases with clinical symptoms of cervical shortening after Cx. Effect of Pg on SPTB in woman with Cx may be evaluated with a randomized controlled trial.