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Combining pessary, cerclage and vaginal progesterone to prevent preterm birth: Why not?

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Introduction

Preterm birth is one of the major unresolved obstetrical issues in the world. It affects both developing and developed countries and leads to poor maternal and fetal outcomes. Prevalence of preterm birth varies between 3–6 % across countries [1].

To date, the most studied prophylactic treatments for preterm birth are two mechanical devices: cervical pessary and cerclage, and one hormonal medication: vaginal or intramuscolar progesterone. Unfortunately, clinical trials have yielded mixed results for each of the aforementioned treatment, for singletons and multiple pregnancies.

Here we briefly summarize the current knowledge about the efficacy of single and combined treatments to prevent preterm birth, and we present our innovative proposed combination of treatments using cervical pessary, cerclage and progesterone at the same time.

Single treatment

In November 2018 Medley et al. summarized the Cochrane reviews about the interventions to prevent preterm birth. They did not find any clinically important intervention with cervical pessary and vaginal progesterone because the Cochrane Reviews were not current [2]. They state that all of these interventions are still current fields of research. At the same time, no Cochrane systematic review reported clear harm, which mean that they are all safe interventions for mother and babies.

In February 2018 two of the most important American and European research groups, summarized with an important review all the findings about progesterone and preterm birth, showing that vaginal progesterone decreases the risk of preterm birth and improves perinatal outcomes in singleton gestations with a short cervical length [3].

A successive review by Sykes et al. in October 2018 states there is lack of consistency in the reported beneficial effects of progesterone for the prevention of preterm birth and improvement in neonatal outcome [4].

Regarding the cervical pessary, Saccone et al. in 2017 in a meta-analysis found that in singleton pregnancies with a midtrimester short cervix the cervical pessary does not reduce the rate of spontaneous preterm delivery or improve perinatal outcome [5].

In a Cochrane systematic review dated 2017, Alfirevic et al. found out that cervical cerclage reduces the risk of preterm birth in women at high-risk of preterm birth and probably reduces risk of perinatal deaths [6].

As outlined by a recent review by Murray et al. of January 2018, cervical cerclage reduces preterm birth rates in singletons but has mixed results in twins with some studies showing harm [7]. The use of progesterone to prevent preterm birth has not been proven to be efficacious in twins. Whether the cervical pessary is effective in preventing preterm birth in multiple pregnancies is still a matter of debate.

Combination of treatments

In UK, after the introduction of the new NICE guidelines and the creation of specialized preterm labor prevention units, there has been a change from almost 50% of the clinics offering cerclage as treatment for short cervical length to offering more choices between cerclage, vaginal progesterone or pessary and a combinations of them.

In singletons, in December 2017 a systematic review and metanalysis by Jarde et al. showed no differences when combining multiple methods to prevent preterm birth [8].

A prospective randomized trial by Enakpene et al. in October 2018 reported a reduction in preterm birth in the group treated with cerclage and vaginal progesterone vs vaginal progesterone alone, in singletons with mid-trimester short cervix [9].

In October 2018, Eke et al. reviewed the current literature and reported that intramuscular 17−OHPC in combination with prophylactic cerclage in women with prior preterm birth had no synergistic effect in reducing spontaneous recurrent preterm birth or improving perinatal outcomes [10].

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In twins, the combination of multiple single treatments has not been extensively studied. In May 2018 a retrospective study by Zimerman et al. compared twin pregnancies with short cervical length treated with combined treatment of cervical pessary and vaginal progesterone to a control group with conservative treatment for the prevention of preterm [11]. The treatment group had a lower incidence of preterm birth before 28 weeks [11]. Definitely more studies are needed to assess preterm birth prevention efficacy of combination of treatments in twins.

Our idea: to combine three treatment at the same time

We propose the initiation of new clinical trials with the use of cervical pessary, cerclage and vaginal or intramuscolar progesterone at the same time. Single and combined treatments have been studied before, but nobody has ever applied cerclage and pessary at the same time on a patient.

As mentioned before, these single treatments are considered safe with no evidence of harm for the patients. Single treatments have failed to uniformly give evidence of efficacy in preventing preterm birth, and combined treatment have been only studied in a limited way.

In fact, previous results obtained with the combination of two of the treatments do not apply when the treatments become three, so previous studies have only limited value when pondering the initiation of this innovative treatment.

Logistically, the cervical cerclage would perfectly fit inside the hole of the pessary and their efficacy could be boosted by the progesterone medication.

We encourage research groups to try this new technique and we remain available for any guidance and support needed.

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