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Cervical Pessary Use and Preterm Birth

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Abstract: Preterm birth remains a considerable public health concern and priority. Little headway has been made in the prevention of preterm birth despite considerable research in this area. New ideas and treatments are desperately needed. The pessary has emerged as a possible treatment for the prevention of preterm birth in both singleton and twin gestations. It appears to be low cost with minimal side effects. This review focuses on the available evidence for the use of cervical pessaries for the prevention of preterm birth, especially in a high-risk population with a shortened cervical length. Larger scale randomized-controlled trials are warranted before incorporation of the pessary into standard obstetrical practice.
Key words: cervical pessary, preterm birth, cervical length, cerclage, twins

Introduction

Preterm birth remains a considerable public health concern and priority. The preterm birth rate in the United States increased 30% in the last several decades, peaked at 12.8% in 2006, and declined only slightly to 11.7% in 2011.[1,2] Preterm birth is not only a leading cause of neonatal mortality, but also a considerable cause of both short-term and long-term morbidity in survivors.[3] Despite efforts in research and treatment, little headway has been made in the prevention of preterm birth. Continuing research for new ideas and treatments for preterm birth prevention are not only desirable but remain desperately needed.

Spontaneous preterm birth comprises 65% of all preterm deliveries and is also the most common cause of extremely preterm and periviable births.[4] Preterm birth is thought to result from any number of complex heterogeneous pathways. Spontaneous preterm birth may follow uterine contractions, preterm premature rupture of membranes, cervical shortening, or some combination of these events. Just as the pathways to preterm birth are complex, the potential mechanisms leading to activation of the pathways are complex and may include a number of factors including upper genital tract colonization or infection, decidual hemorrhage, mechanical weakness of the cervix, as well as a number of other factors.[5]

One of the strongest risk factors for a preterm birth is a history of a prior preterm birth, and we have learned much about potential therapies to reduce the likelihood of recurrent preterm birth over the last decade.[6] Intramuscular 17

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α-hydroxyprogesterone caproate (17-OHP) administered weekly from 16 to 36 weeks reduces the risk of preterm birth in this population of patients by approximately 35%.[7] Other studies have evaluated the use of vaginal progesterone in women with prior spontaneous preterm birth and found similar reductions in preterm birth, especially in those with a short cervix.[8,9]

A cervical length measuring < 25 mm (10th percentile for singleton gestations) diagnosed by transvaginal ultrasonography in the midtrimester (16 to 24 wk) is a powerful predictor of recurrent preterm birth in women with a prior preterm birth.[10,11] A recent randomized-controlled trial demonstrated that placement of a cerclage in women with a prior spontaneous preterm birth who have a cervical length of < 25 mm reduces periviable birth and perinatal mortality. Moreover, in women with a cervical length < 15 mm, cerclage reduced the rate of preterm delivery prior to 35 weeks.[11–13] With the benefit of an intervention, women with a history of a prior spontaneous preterm birth are now typically offered cervical length screening in a subsequent pregnancy starting at 16 weeks' gestation.[14]

Although progesterone, cervical length screening, and cerclage placement for cervical shortening are the current interventions aimed at reducing recurrent preterm birth in a high-risk population, there are fewer proven strategies for nulliparous or otherwise lower risk women. Given its availability, cervical shortening has been utilized as a mechanism for identifying women who would otherwise be at low risk for spontaneous preterm birth and for whom interventions might be beneficial. Although the utility and cost-effectiveness of universal cervical length screening in a nulliparous population remains somewhat controversial, cervical pessary, vaginal progesterone, and 17-OHP have all been studied as treatment options for women with a sonographically detected short cervix. Several studies have shown a reduction in preterm birth in women with a short cervix treated with vaginal progesterone,[8,9,15] but there has been a tremendous interest in the use of a pessary for women with a short cervical length.[16] Using a meta-analytic approach, Alfirevic and colleagues compared pregnancy outcomes in women with a singleton pregnancy, a history of a prior preterm birth, and a short cervix diagnosed by ultrasound who were treated with either vaginal progesterone, cerclage, or pessary in different clinical trials. Although this not a direct comparison of methods, neonatal morbidity and the rate of preterm births were similar between the 3 groups.[17] Given the low cost and potential effectiveness of a pessary for the prevention of preterm birth, this review focuses on the rationale for, potential mechanisms of, and available evidence on the use of pessaries for the prevention preterm birth.

Pessaries

Vaginal pessaries are most well known for their role in incontinence and pelvic organ prolapsed.[18,19] Most pessaries are made of flexible silicone or plastic so that they can be compressed and easily inserted. Pessaries are available in a number of different sizes and shapes, and when utilized for pelvic organ prolapse, the shape is typically determined based on the type and extent of the pelvic floor defect. When utilized for obstetric indications, the pessaries most commonly reported in the literature are the Hodge/Smith-Hodge and the Arabin pessaries. The Arabin pessary is applied around the cervix and fits at the level of the internal os, whereas the Hodge pessary is typically fitted so that it sits just below the cervix elevating and potentially flexing it.

The use of a pessary for the treatment of cervical insufficiency is not a new concept, but renewed interest in its use has developed over the past several years since

the publication of recent European trials suggesting efficacy in preventing preterm birth, especially in selected populations with a shortened cervical length.[16] More recent studies have focused on the Arabin pessary. Its recent popularity also stems from the fact that it is inexpensive and easily inserted and removed in the practitioner's office without the need for anesthesia. Moreover, the avoidance of medication exposure, especially hormone exposure, has helped drive interest in pessary as a treatment modality.

Potential Mechanisms

Although the exact mechanism responsible for reducing the likelihood of preterm birth is unknown, several hypotheses explaining the potential mechanism of action exist. One theory is that the pessary works through a mechanical approach by changing the uterocervical angle and displacing it more posteriorly. This directs weight and pressure away from the internal os and instead displaces it onto the anterior lower uterine segment.[16,19–22] Ultrasound examinations and magnetic resonance imaging have demonstrated this change in angle.[22,23] In fact, Cannie and colleagues showed that the degree of change in the uterocervical angle may actually be associated with the likelihood of preterm birth. Using magnetic resonance imaging, they measured the uterocervical angle before and immediately after placement of the Arabin pessary; women who delivered after 34 weeks had a significantly more acute uterocervical angle after pessary placement compared with those that delivered before 34 weeks.[23] In addition to changing the uterocervical angle, the Arabin pessary may also prevent opening of the internal cervical os due to its shape and location of placement.[21]

In addition to a mechanical function, pessaries may also impact the biochemical and microbiological environment of the cervix. Because of pressure on the cervix, several authors have suggested that a pessary may protect and prevent deterioration of the mucous plug, which has been shown to protect against ascending infection.[21,24,25] Whether or not the pessary changes the cervicovaginal microbial milieu in some way that offers protection from infection and preterm birth is unknown. Further studies are needed to fully examine potential changes in the cervicovaginal microbial environment due to the pessary.

Pessary Use to Prevent Preterm Birth

One of the first reported cases of the use of a ring pessary for the treatment of cervical insufficiency, called the Bakelite ring, was described by Cross in 1959 in the *Lancet*.

Of the 13 patients with a history of a second trimester loss because of either incompetent cervix, cervical laceration, or Mullerian abnormality who were treated with a pessary, 8 had full-term births.[26] In 1963, Vitsky used the Smith-Hodge pessary in 21 patients with cervical incompetence and reported term deliveries in 66%.[27,28] Oster and Javert[29] reported similar success with the Hodge pessary in 29 patients with cervical incomepetence.

Arabin and colleagues published a nonrandomized study examining whether the vaginal ring pessary decreased the rate of spontaneous preterm birth in women at high risk for a spontaneous preterm birth—defined as either a history of spontaneous preterm birth or symptoms of preterm labor in the current pregnancy and a cervical length of ≤ 15 mm. Twelve patients with singleton pregnancies underwent pessary placement and were compared to controls matched for gestational age. The women who received pessary delivered at 38 weeks compared to 33 weeks for women without a pessary.[30]

Acharya and colleagues also evaluated the safety and efficacy of the Arabin ring cervical pessary for treating cervical

shortening. Women underwent transvaginal ultrasound screening for a number of indications: (1) a prior second trimester pregnancy loss; (2) a prior preterm delivery < 34 weeks; (3) a prior cervical cone procedure; or (4) a multiple gestation. Placement of a cervical pessary was offered to women found to have a cervical length of ≤ 25 mm. Cervical length screening was performed every 2 to 3 weeks after 17 to 19 weeks and a pessary was placed up to 30 weeks' gestation. Overall, 32 patients had a cervical pessary placed (9 with twin gestations and 2 with triplet gestations), and 3 required early delivery for obstetrical indications. For the remaining 29, the average time from pessary insertion to delivery was 10.4 weeks and the average gestational age at delivery was 34 weeks among all patients; in a subgroup analysis of singleton gestations, the average gestational age of delivery was 35 weeks with an interval from pessary insertion to delivery of 11.7 weeks.[31]

In another nonrandomized study, Sieroszewski and colleagues reported outcomes of 54 patients with a cervical length between 15 and 30 mm who had an Arabin cervical pessary placed before 28 weeks' gestation after a diagnosis of a short cervix. The mean gestational age at insertion was 20 weeks. The overall mean gestation age at delivery was 35.3 ± 4.4 weeks and the mean duration from time of pessary insertion to time of delivery was 15.7 ± 5.4 weeks. Overall, 83% of women who had had a pessary placed delivered at > 37 weeks' gestation.[32]

Although the earlier studies were highly suggestive of benefit with use of a pessary in the setting of cervical shortening, a Cochrane review published in 2010 failed to identify any clinical trials evaluating pessary that met inclusion criteria and therefore the authors could not "confirm or refute the benefit of the cervical pessary."[33] The first randomized-controlled trial to assess its effectiveness was published by Goya et al in 2012.[16]

The Pesario Cervical para Evitar Prematuridad (PECEP) trial was conducted by Goya and colleagues at 5 different hospitals within Spain. Pregnant women were offered cervical length screening during their routine second trimester anatomy ultrasound. Those with a cervical length ≤ 25 mm were offered entry into PECEP. Participants were randomized to either the Arabin cervical pessary or no cervical pessary. The primary outcome of this trial was spontaneous preterm birth before 34 weeks of gestation and a total of 385 women were enrolled. A total of 192 were randomized to pessary and 193 to expectant management. The women in the pessary group had a dramatic reduction in the rate of spontaneous preterm birth in < 34 weeks compared with the expectant management group [6% vs. 27%; odds ratio, 0.18; 95% confidence interval (CI), 0.08-0.37] (Table 1). The expectant management group was also more likely to receive tocolytic therapy and corticosteroid treatment for threatened preterm labor, whereas neonates born to mothers in the pessary

TABLE 1. PECEP Trial: Pregnancy Outcomes[16]

	Cervical Pessary (n = 190)	**Expectant Management (n = 190)**	**OR (95% CI)**	***P***
SPTD < 28 wk [n (%)]	4 (2)	16 (8)	0.23 (0.06-0.74)	0.0058
SPTD < 34 wk [n (%)]	12 (6)	51 (27)	0.18 (0.08-0.37)	< 0.0001
SPTD < 37 wk [n (%)]	41 (22)	113 (59)	0.19 (0.12-0.30)	< 0.0001
Gestational age at delivery (wk)	37.7 (2.0)	34.9 (4.0)		< 0.0001

CI indicates confidence interval; OR, odds ratio; SPTD, spontaneous preterm delivery.

group were less likely to weigh < 2500 g, develop sepsis or respiratory distress syndrome, or develop the composite adverse neonatal outcome.[16]

Side Effects

In all of the published reports of pessary use, there have been no serious side effects reported as a result of cervical pessary use. The most common side effects reported include an increase in vaginal discharge and pain during insertion and removal of the pessary. No significant complaints of daily pain or serious vaginal bleeding have been reported, and overall the pessary seems to be well tolerated by patients. Arabin and colleagues administered patient questionnaires in their original pilot study. Although complaints of vaginal discharge increased after pessary placement, no patients complained of pain once the pessary was in place. Pain during insertion was reported in 3 of 12 patients with an average score of 5 on a scale of 0 to 10; pain during removal was reported in 4 of 12 patients with an average score of 6 on a scale of 0 to 10.[30] In the study by Acharya and colleagues, the authors reported no significant complications as a result of the use of the pessary, although 2 women had the pessary removed due to discomfort and constipation. They reported no complications with pessary removal or insertion.[31]

Patients in the PECEP study completed satisfaction questionnaires regarding the cervical pessary and side effects. Overall, 95% of the patients in the pessary group would recommend its use to others. No serious side effects were reported with the use of the pessary. Vaginal discharge was reported in all patients treated with a pessary, versus 46% of patients in the expectant management group. This increase in vaginal discharge is consistent with other studies. The increase in vaginal discharge seems to be most related to a benign foreign body reaction as it is not associated with development of any specific pathogenic condition or infection of the lower genital tract. There was no increase noted in the incidence of vaginal infections or chorioamnionitis in the pessary group. Similarly, there was no association between pessary use and incidence of heavy bleeding, cervical tear, or uterine rupture.[16] Although the increase in vaginal discharge prompted more evaluations for membrane rupture, use of the pessary was not associated with membrane rupture. The rate of premature rupture of membranes was actually higher in the expectant management group (2% vs. 9%). Overall, 14% of patients required pessary repositioning without removal and 1% required pessary removal and replacement. Pain during pessary insertion was ranked as a 4 on a scale of 1 to 10 and pain during removal was ranked as a 7 according to the patient satisfaction questionnaire.[16] Similar side effects were observed in the ProTWIN trial. Twenty-six percent of 401 patients in the pessary group reported vaginal discharge as expected. Pain was reported in 4% and both pain and discharge was reported in 3% of pessary patients.[34]

Multiple Gestations and Pessary Use

Multiple gestations are at an increased risk of preterm labor and delivery, with the average gestational age at delivery declining with each additional fetus present. The average gestational age at delivery for twin gestations is 36 weeks and for triplets 34 weeks. Although there have been several well-studied interventions in singletons to prevent preterm birth, they have not shown the same benefit in multiple gestations, particularly twin gestations.

Despite its effectiveness in singleton pregnancies with a history of a prior preterm birth, the use of 17 α-hydroxyprogesterone caproate has not been shown to be effective in decreasing the

TABLE 2. ProTWIN Trial: Pregnancy Outcomes for All Types of Twins[34]

	Cervical Pessary (n = 401)	Control Group (n = 407)	RR (95% CI)
SPTD < 28 wk [n (%)]	16 (4)	16 (8)	0.79 (0.50-1.27)
SPTD < 32 wk [n (%)]	41 (10)	51 (27)	0.86 (0.65-1.15)
SPTD < 37 wk [n (%)]	222 (55)	113 (59)	0.94 (0.87-1.07)
Gestational age at delivery (wk)	36.7 (34.7-37.4)	36.4 (34.3-37.6)	0.91 (0.76-1.09)*

*HR (95% CI).

CI indicates confidence interval; HR, hazard ratio; RR, relative risk ; SPTD, spontaneous preterm delivery.

rate of preterm birth in patient with twin or triplet gestations, even in those with a cervical length of < 25 mm.[35–37] Similarly, although cerclage reduces the rate of preterm birth in singleton pregnancies with a history of a prior preterm birth and a cervical length < 25 mm, it may actually be harmful in twin gestations, increasing the risk of preterm birth and perinatal mortality.[12] Although vaginal progesterone has shown some promise in twin gestations with shortened cervix, the data are limited and larger randomized trials are needed to study the potential benefits in this population.[38–40]

Similar to the findings of the use of vaginal progesterone in multiples, the use of a cervical pessary in selected groups of twin gestations has shown some promise. The ProTWIN trial recently examined the effectiveness of cervical pessary for preventing preterm birth in multiple gestations. A total of 813 women with a multiple pregnancy between 12 and 20 weeks' gestation were randomized to the Arabin pessary or a control group. Overall, the prophylactic use of the pessary did not decrease the incidence of a composite of poor perinatal outcomes nor did it decrease the incidence of preterm birth prior to 32 or 37 weeks' gestation[34] (Table 2). However, in a subgroup analysis of women with a cervical length of < 38 mm (the 25th percentile of cervical length in this trial), those treated with a pessary had a significant reduction in the incidence of a composite of poor perinatal outcomes (12%) versus the control group (29%) (relative risk, 0.40; 95% CI, 0.19-0.83). In addition, the mean gestational age at delivery was greater in the pessary group compared with the control group, 36.4 versus 35.0 weeks, (relative risk, 0.49; 95% CI, 0.32-0.77). There was also a decreased incidence of delivery before 28 and 32 weeks' gestation (Table 3).

The data from the recent trials on twins show promise, but the findings need to be confirmed in larger randomized trials. Given that other interventions have not been shown to be effective, further studies are warranted examining the use of the cervical pessary in multiple gestations, especially those at highest risk with a shortened cervical length. No definitive conclusions and recommendations about

TABLE 3. ProTWIN Trial: Pregnancy Outcomes for Twins With Cervical Length of < 38 mm[34]

	Cervical Pessary (n = 78)	Control Group (n = 55)	RR (95% CI)
SPTD < 28 wk [n (%)]	3 (4)	9 (16)	0.23 (0.06-0.87)
SPTD < 32 wk [n (%)]	11 (14)	16 (29)	0.49 (0.24-0.97)
SPTD < 37 wk [n (%)]	50 (64)	43 (78)	0.82 (0.54-1.24)
Gestational age at delivery (wk)	36.4 (35.0-37.3)	35.0 (30.7-36.7)	0.49 (0.32-0.77)*

*HR (95% CI).

CI indicates confidence interval; HR, hazard ratio; RR, relative risk; SPTD, spontaneous preterm delivery.

the benefit of the pessary in this group can be made until further larger scale studies are performed.[41]

Cervical Length Measurement After Pessary Placement

Although there are no data supporting assessment of cervical length after pessary placement, some clinicians want to be able to periodically reassess patients without removing the pessary. Goya et al[22] published their method of obtaining cervical lengths with the cervical pessary left in place. Cervical lengths are typically obtained through a transvaginal approach rather than a transabdominal approach given the difficulty obtaining an accurate view of the cervix transabdominally, particularly in an obese population, but because the position of the pessary interferes with the usual transvaginal imaging technique and visualization, modification is required. Goya and colleagues described a technique utilized in 43 patients with a cervical pessary where the ultrasound probe is placed just inside the cervical pessary flush against the external os, enhancing visualization of the entire cervical canal. Interobserver differences in the measurements were minimal, and only 1 patient was unable to tolerate cervical length measurement because of discomfort.[22]

Conclusions

The cervical pessary has been shown in recent European trials to be efficacious at preventing preterm birth, especially in a high-risk population of women with a shortened cervical length. The pessary is easily inserted and removed without the need for anesthesia. It appears to be well tolerated by patients with no reports of serious adverse side effects as a result of its use. However, before the cervical pessary can be recommended as part of standard obstetrical practice and added to the armamentarium for prevention of preterm birth, larger scale randomized-controlled trials are warranted, especially in women with shortened cervical lengths and multiple gestations.

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