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Use of Cervical Pessary in the Management of Cervical Insufficiency

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Abstract: Prevention of spontaneous preterm birth is an important public health priority. Pessary may be a potential therapy in cases of cervical insufficiency, in singleton and multiple gestations. Availability of transvaginal sonography for accurate assessment of cervical length is allowing for the tailoring of therapy to a more specific subset of patients who may benefit from this treatment. Pessary therapy is attractive given the favorable side effect profile, low cost, and ease of placement and removal. Large randomized trials are ongoing to validate initial favorable findings.
Key words: cervical insufficiency, cervical pessary, cerclage, preterm birth, cervical length

Introduction

The strongest predictors of preterm birth are prior preterm delivery and midtrimester short cervical length. Current strategies for preterm birth prevention are medical (progesterone treatment), surgical, or a combination of both (ultrasound-indicated cerclage placement for women with progressive cervical shortening despite treatment with intramuscular progesterone and a history of prior preterm birth).

Cervical pessary (barrel-shaped ring, Fig. 1) has promise as an alternative (or potentially adjunctive) treatment for women with cervical insufficiency and is an attractive option given that it is noninvasive, easy to use, low cost, does not require anesthesia, and can be easily placed and removed in an ambulatory setting.

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The author declares that there is nothing to disclose.

Potential Mechanisms of Action

The exact mechanism of action of the pessary remains unclear. Vitsky,[1] in 1961, speculated that posterior deviation of the cervix and redistribution of the uterine weight were the results of pessary placement. Oster and Javert[2] also suggested that the pessary corrects the angle of the cervix, pointing it posteriorly, and

FIGURE 1. Barrel-shaped pessary (Bioteque America Inc., San Jose, CA).

prevents cervical dilation by direct pressure at the level of internal cervical os. Rotation of the cervix to the posterior vaginal wall was also proposed by Arabin et al[3] as a possible mechanism, with redistribution of uterine weight onto the anterior portion of the lower uterine segment, rather than directly over the cervix. Study by Cannie and colleagues evaluated cervical appearance and position using serial magnetic resonance imaging (MRI) after insertion of an Arabin pessary in women carrying a singleton pregnancy with a cervical length of 25 mm or less between 17 and 31 weeks (n = 54). An MRI was performed immediately before and after placement of the pessary and at monthly follow-up. The authors found a mechanical effect on the uterocervical angle, with a much more acute angle than before placement; however, the cervical displacement appeared to occur more anteriorly, rather than posteriorly, resulting in cervical kinking. Cervical edema was also noted to develop over time that may confer additional protections against preterm birth. The authors also proposed that the pessary could cause displacement of the internal cervical os posteriorly, toward the spine, which would alter gravity effects at the internal os.[4] Although this was a very interesting study and the first objective evaluation of one of the proposed mechanisms of action of the pessary, the conclusion that appropriate placement of the pessary can be confirmed by "quickly and easily using MRI" is difficult to apply in a nonresearch setting.[4] Goya et al[5] suggested that the pessary may support the immunologic barrier between the chorioamnion-extraovular space and the vaginal microbiological flora, potentially protecting the mucus plug.

Overview of the Literature

SINGLETON GESTATION

Although pessaries are widely used for treatment of pelvic organ prolapse, they are not currently FDA approved for treatment of cervical insufficiency. The first report of pessary use in 13 obstetric patients was described by Cross[6] in 1959, who used a Bakelite ring pessary inserted to the level of internal os, and reported 8 full-term deliveries, 2 failures, and 3 ongoing pregnancies at 12, 24, and 36 weeks. Indications for pessary use in these patients included cervical insufficiency, cervical lacerations, and uterine didelphys. Vitsky[1,7,8] reported his experience with the use of Smith, Hodge, and Risser pessaries in 1961, 1963, and 1968. In 1961, a Smith pessary was used in 3 patients with cervical insufficiency. Before treatment with the pessary, these patients had 6 pregnancy losses before 20 weeks and 4 losses between 24 and 28 weeks. In the next 5 pregnancies, the women were treated with a Smith pessary with 4 of them achieving full-term delivery.[1] This report was followed by a

1963 publication of a case series of 21 patients treated with the Smith-Hodge pessary.[7] Before treatment, there were 24 losses before 24 weeks and 19 living children (23%) among 83 pregnancies. After treatment, there were 21 pregnancies with 2 losses from 20 to 24 weeks, 2 deliveries between 28 and 32 weeks, 3 deliveries at 32 to 36 weeks, and 14 term deliveries, with 18 living children (86%). Three more cases were described in 1968 using a Hodge pessary in 2 patients and a Risser pessary in the third, all with favorable outcomes.[8]

Oster and Javert[2] published the largest case series at that time in 1966, describing the use of a Hodge pessary in 29 patients with 35 pregnancies. Before treatment with the pessary, 94 pregnancies resulted in 21 living children (22%). After treatment with the pessary, 29 of 35 pregnancies resulted in live births (83%), with 65% of deliveries occurring at term, compared with 17% before treatment.

Early reports of pessary use, although promising, were limited by small sample size, methodological issues, unclear inclusion criteria, and difficulty with objective diagnosis of cervical insufficiency. For example, in the original report by Cross,[6] 2 of the patients with a diagnosis of "deficient internal os" had 5 losses before 12 weeks, which although indicative of recurrent pregnancy loss, is not necessarily diagnostic of cervical insufficiency.

In 2003, Arabin et al[3] published a prospective pilot study evaluating a cervical pessary specifically designed for reduction of spontaneous preterm birth. Between 1997 and 2001, the authors performed transvaginal ultrasound on all singleton and twin pregnancies with risk factors (prior history of spontaneous preterm birth before 36 wk or symptoms of cramping and pressure). Beginning in 1998, patients with a cervical length of 15 mm or less between 22 and 24 weeks were offered treatment with an Arabin pessary, with 12 singleton and 23 twin pregnancies treated. Among the first 11 patients treated (4 singletons and 7 twins), no delivery occurred before 32 weeks. The authors then performed a retrospective matched-pair analysis, utilizing 12 singleton and 23 twin controls selected from the database, matching the cervical length within 2 mm at the same gestational week as the prospectively treated subjects, from 18 to 28 weeks. In 12 singleton pregnancies treated with the pessary, there were no cases of spontaneous preterm birth, compared with 6/12 controls, with 25% delivering before 32 weeks. In twin pregnancies treated with the pessary, 8/23 had spontaneous preterm birth with no deliveries before 32 weeks, whereas in the control group, 12/23 delivered preterm with 30% before 32 weeks.

Acharya et al[9] conducted a prospective study that included 32 women with a cervical length of 25 mm or less before 30 weeks, managed with a cervical pessary, including 9 twin and 2 triplet pregnancies. The goal was to evaluate the efficacy and safety of cervical pessary use in the treatment of cervical insufficiency. Interval between pessary placement and delivery ranged from 2 to 19 weeks, with an average of 10.4 weeks, with 45% of women delivering before 34 weeks. Subgroup analysis of pregnancies with multiple gestation showed a shorter pessary to delivery interval of 7.4 versus 11.7 weeks, with an average gestational age at delivery of 30 versus 35 weeks for singletons. Prolongation of pregnancy beyond 32 weeks was achieved in 56% of patients. The study, although prospective, is limited by small sample size and lack of control group.

The use of Arabin pessary was described in patients with a cervical length between 15 and 30 mm before 28 weeks with 83.3% of women delivering after 37 weeks.[10] The findings, however, are difficult to interpret given inclusion of patients with longer cervical lengths, and treatment of all patients with vaginal progesterone, which has been shown to decrease the risk of spontaneous

preterm birth when used as a sole treatment in patients with a short cervical length.[11,12] In the United States, the recommended treatment for patients with a prior history of spontaneous preterm birth is 17-α-hydroxyprogesterone and ultrasound-indicated cerclage placement should the cervical length decrease to < 25 mm (if the qualifying birth occurred before 34 wk), as an adjunct treatment to progesterone.[13] Women without a history of prior preterm birth and cervical length of 20 mm or less are candidates for vaginal progesterone treatment.[13] Data are limited on use of pessary as an adjunct treatment, either with progesterone or cerclage. A recent publication of preintervention and postintervention cohort study by Stricker and colleagues reported on adjunct use of vaginal progesterone (200 mg suppositories) and Arabin cervical pessary in women at high risk defined by a history of spontaneous preterm birth, conization, or cerclage in prior pregnancy and with a cervical length of < 10th percentile in the current pregnancy. There were no differences between pessary plus progesterone group versus pessary alone group in the rate of preterm birth < 34 weeks (32.1% vs. 24.5%, $P = 0.57$); however, the length of stay in the neonatal intensive care unit was shorter in the combined treatment group versus pessary group (46.5 vs. 52 d, $P < 0.001$), although no differences were noted in the composite adverse neonatal outcome.[14] Pessary use as an adjunct to rescue cerclage was retrospectively reviewed by Kosinska-Kaczynska and colleagues—15 women were treated with pessary in addition to cerclage, and 17 women were treated with cerclage alone. Both groups also received vaginal progesterone until 34 weeks. The authors found a significantly later gestational age at delivery with adjunct pessary use (34.7 vs. 29.7 wk, $P = 0.03$), and a longer period between cerclage insertion and delivery (82.9 vs. 52.1 d, $P = 0.045$).[15] Adjunctive treatment with a pessary may be considered in a select group of women who are already receiving vaginal progesterone and continue to have progressive cervical shortening, or who are not deemed to be a candidate for physical examination–indicated or ultrasound-indicated cerclage placement.

Another small study by Ting et al[16] reported results of treatment of 20 women with a cervical length of < 25 mm with Arabin pessary, with a mean prolongation of 11.5 weeks, with 12/20 (60%) patients delivering after 34 weeks. In a subset of women with a cervical length of < 15 mm, 46% delivered after 34 weeks versus 86% of patients with a cervical length of 15 mm or more. The authors suggested that the pessary may not be as effective an option for treatment at lower cervical lengths (< 15 mm).

Two well-designed randomized controlled studies, performed by Goya et al[5] and Hui et al,[17] reported contradictory findings. The Pesario Cervical Para Evitar Prematurida (PECEP) study was a multicenter open-label randomized controlled trial (RCT) conducted in Spain from 2007 to 2010, enrolling patients with a cervical length of 25 mm or less.[5] After screening, 385 patients were randomly allocated to an Arabin cervical pessary versus expectant management at 20 to 23 weeks of gestation. The authors found a significant reduction in spontaneous preterm birth before 34 weeks in the pessary group [6% vs. 27%; odds ratio (OR), 0.18; 95% confidence interval (CI), 0.08-0.37]. Additional findings also included statistically significant reduction in the rate of spontaneous preterm birth before 28 weeks (OR, 0.23; 95% CI, 0.06-0.74) and 37 weeks (OR, 0.19; 95% CI, 0.12-0.30), birth weight < 1500 g (OR, 0.31; 95% CI, 0.13-0.72) and 2500 g (OR, 0.23; 95% CI, 0.12-0.43), respiratory distress syndrome (OR, 0.20; 95% CI, 0.06-0.55), treatment for sepsis (OR, 0.24; 95% CI, 0.04-0.90), and composite adverse neonatal outcomes (OR, 0.14; 95% CI, 0.04-0.39). There was also a significantly higher need for tocolysis and betamethasone administration in the expectantly managed group.[5]

At approximately the same time, another randomized trial was ongoing in China.[17] This study enrolled women from 20 to 24 weeks gestation with randomization for pessary placement if the cervical length was < 25 mm. Original sample size calculations required 1120 patients to show a reduction in spontaneous delivery before 34 weeks from 8% to 4%. As enrollment was slow from 2008 to 2011, the authors performed an interim analysis, evaluating outcomes in 108 women (53 in the pessary group and 55 in the control group). The authors found no difference in the rate of delivery before 34 weeks (9.4% vs. 5.5%, $P = 0.46$), neonatal birth weight (2840 vs. 2953 g, $P = 0.38$), or any other neonatal outcomes in the pessary versus control group, respectively.

Both studies have limitations and underscore the need for large high quality adequately powered randomized trials. The PECEP study has the largest sample size and adequate methodology. Both studies reported a similar incidence of cervical length < 25 mm, 6% in the PECEP study and 4.6% in the study by Hui and colleagues.[5,17] The PECEP study, however, has been criticized due to unusually high spontaneous preterm birth rate in the expectantly managed group as compared by the study by Hui et al[17] (27% vs. 6% before 34 wk and 59% vs. 18.2% before 37 wk).[5] The largest limitation to the study by Hui et al,[17] is small sample size, resulting in a potential lack of power to detect differences, given that the interim analysis was on the basis of < 10% of originally planned patient enrollment. The studied populations also differed in demographics. In the study by Hui and colleagues, patients had lower body mass index (21.7-22.9 vs. 24.5-24.9 kg/m^2) and lower rates of smoking (1.9%-5.5% vs. 19%-20%).

Alfirevic et al[18] compared the use of vaginal progesterone, cerclage or cervical pessary for prevention of preterm birth in women with a prior history of preterm delivery at < 34 weeks and sonographically short cervix. The 3 different cohorts used for comparison were from several sources: 142 US women treated with cerclage placement if cervical length was < 25 mm (with or without 17-α-hydroxyprogesterone), 59 UK women treated with vaginal progesterone if cervical length was less than the third percentile (with cerclage placement in cases of continued decrease in cervical length to < 15 mm), and 42 women from Spain treated with a cervical pessary. The authors found no statistically significant differences in neonatal morbidity, perinatal losses, and preterm births, or birth before 34 weeks when comparing women with cervical length of < 25 mm. These findings suggest similar effectiveness of 3 treatment options for women with prior spontaneous preterm birth and sonographically detected short cervix. The limitations of this study include indirect comparison of these interventions, as the cohorts of patients were pooled from 3 different studies with different methodologies, patient populations, and hence different rates of preterm birth.

MULTIPLE GESTATION

Data are very limited for the use of pessary in twin gestations, with only a small number of patients evaluated in older studies. Carreras et al[19] reported on the use of an Arabin pessary to prevent preterm birth in severe twin twin transfusion syndrome treated with laser surgery. This was a retrospective analysis of a consecutive series of 79 cases with severe twin twin transfusion syndrome; cervical length > 25 mm (group A, n = 63) versus 16 patients with cervical length ≤ 25 mm [8 underwent expectant management (group B) and 8 treated with pessary placement (group C)]. The expectantly managed group B was treated as per routine prematurity prevention protocols including tocolysis if indicated. The authors found that median gestational age at delivery was significantly higher in groups C versus B (32 vs. 28 wk, $P = 0.01$), with a decrease in severe neonatal morbidity in groups C

versus B (18% vs. 70%, $P = 0.01$). The study was limited by small sample size and the use of historical cohort for expectantly managed group with a cervical length > 25 mm (group A). The rate of preterm birth for group B was higher than reported previously in the literature, underscoring potential bias in the study.

A study by Acharya et al[9] included 9 twin and 2 triplet pregnancies with cervical length < 25 mm treated with pessary placement, with a mean interval to delivery time of 7.4 weeks and an average gestational age of delivery of 30 weeks.

The first RCT on pessary use in twin pregnancies was published by Liem et al[20] in 2013. The ProTWIN study was a multicenter open-label randomized study conducted in the Netherlands. The authors enrolled women with multiple gestation to pessary or control groups, with insertion of the pessary between 16 and 20 weeks gestation, regardless of cervical length. The primary outcome was a composite of poor perinatal events. The study found no benefit to prophylactic treatment with pessary use in an unselected group of women with multiple gestations (OR, 0.98; 95% CI, 0.69-1.39). The authors also originally planned a subgroup analysis of women with cervical length of < 25 mm; however, that criteria was modified to the 25th percentile for cervical length (38 mm in this patient population) to get adequate sample size, as only 9 women had cervical length < 25 mm. Analysis of the patients with a cervical length of < 38 mm showed less frequent poor perinatal outcome [12% vs. 29%; relative risk (RR), 0.40; 95% CI, 0.19-0.83], later median gestational age at delivery (36.4 vs. 35.0 wk; RR, 0.49; 95% CI, 0.32-0.77), and lower risk of preterm delivery before 28 and 32 weeks (4% vs. 16%; RR, 0.23; 95% CI, 0.06-0.87 before 28 wk and 14% vs. 29%; RR, 0.49; 95% CI, 0.24-0.97 before 32 wk).[20] Economic analysis demonstrated that treatment with a cervical pessary seems to be highly cost-effective in this subgroup of patients.[21]

Two more recently published randomized trials evaluated pessary use in twin gestation.[22,23] Nicolaides and colleagues reported on pessary use in 1180 unselected twin pregnancies and found no significant differences in rates of spontaneous birth < 34 weeks (13.6% vs. 12.9%; RR, 1.054; 95% CI, 0.787-1.413), perinatal death (2.5% vs. 2.7%; RR, 0.908; 95% CI, 0.553-1.491), or adverse neonatal outcome (10.0% vs. 9.2%; RR, 1.094; 95% CI, 0.851-1.407). A post hoc subgroup analysis of 214 women with short cervix (≤ 25 mm) did not find a benefit from pessary treatment: spontaneous birth < 34 weeks (31.1% vs. 25.9%; RR, 1.201; 95% CI, 0.784-1.839), perinatal death (12.3% vs. 5.6%; RR, 2.208; 95% CI, 0.872-5.592), or adverse neonatal outcome (23.2% vs. 19.6%; RR, 1.185; 95% CI, 0.696-2.016).[22] Goya and colleagues' PECEP-twins study was a multicenter open-label RCT in Spain, enrolling 137 women with cervical length ≤ 25 mm. The findings were in contrast to those of Nicolaides, with spontaneous preterm birth < 34 weeks significantly less frequent in the pessary group than in the expectantly managed group (16.2% vs. 39.4%; RR, 0.41; 95% CI, 0.22-0.76), with a significant reduction in the rate of birth weight < 2500 g (RR, 0.72; 95% CI, 0.54-0.97). The authors concluded that in selected twin pregnancies with short cervix ≤ 25 mm, pessary placement at 22 weeks significantly reduces the rate of spontaneous preterm birth at < 34 weeks.[23]

There are currently 9 registered trials on ClinicalTrials.gov evaluating pessary use for treatment of short cervix in twin gestations (accessed March 3, 2016).

Patients Who May Benefit From Pessary Placement

Asymptomatic patients with a short cervical length on transvaginal ultrasound and no prior history of spontaneous

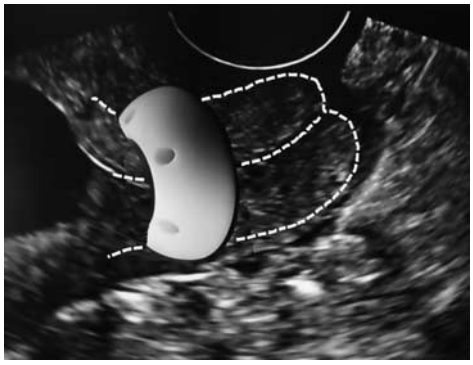

FIGURE 2. Transvaginal sonography of the cervix with graphical representation of theoretical pessary placement.

preterm birth may benefit from treatment with the pessary. In the United States, the recommended treatment is vaginal progesterone should the cervical length decrease to $\leq$20 mm; pessary placement may be considered for an adjunct treatment or in lieu of progesterone depending on patient and clinician preference. A pessary can also be placed in instances when a cerclage is not customarily performed (ie, after 24 wk), or potentially in a twin gestation with cervical length $<$ 25 to 38 mm. A pessary may also be considered as an adjunct to cerclage if continued cervical shortening is documented. A decision to use the pessary as an adjunct treatment should be individualized and is limited by small number of prospective studies, but rather specific clinical situations and anecdotal evidence. All patients receiving treatment with the pessary in the United States outside of a research setting, should be informed of the off-label use of the device.

Technical Aspects of Pessary Placement

Patients who are identified as potential candidates for treatment with a pessary, should be counseled on potential benefits, risks, and alternatives of pessary placement. Informed consent should include discussion regarding current standard of care specific to patient's unique clinical circumstances, review of the current best quality literature and their findings, and understanding that in the United States the use of pessaries for prevention of preterm birth is off-label (Arabin pessary is certified by the European Conformity, CE0482, MED/CERT ISO 9003/EN 46003, for prevention of spontaneous preterm birth in the European Union and other countries, but is not available for sale in the United States).

Pessary placement is easily performed in an office setting with minimal discomfort to the patient.

(1) Perform speculum examination to evaluate cervix and estimate an appropriate size pessary.
(2) Compress the pessary between 2 fingers and apply sterile gel to ease placement.
(3) Place the pessary with the smaller diameter toward the cervix and push up on the pessary to achieve placement as near the internal cervical os as possible (Fig. 2).
(4) Confirm that the cervix is surrounded circumferentially by the inner (narrower) diameter of the pessary.
(5) Apply downward pressure on the proximal anterior edge of the pessary to angle the cervix posteriorly.
(6) Have the patient sit, walk, and void and monitor for discomfort or difficulty voiding.

Studies evaluating cervical pessaries for prevention of preterm birth, did not routinely remove pessaries before 36 to 37 weeks and no special maintenance care was necessary. However, studies do report approximately 15% rate of refitting the pessary for various reasons.[4,5] Any vaginal infections can be treated with the pessary left in situ, and removal is indicated in cases of preterm premature rupture of membranes and preterm labor, or significant patient discomfort.[5] If removal and

reinsertion of the pessary is necessary, the pessary can be washed with water and replaced.[24]

Adverse Effects From Pessary Use

Few complications of pessary use have been reported. Goya et al[5] administered a patient questionnaire with the findings of vaginal discharge reported by all of the patients. Only 1 patient required pessary removal due to discomfort and most patients ranked pain 4/10 on insertion and 7/10 on removal, with 95% of patients recommending the pessary to other people.[5] Similar findings were reported by Arabin et al,[3] with significant increase in vaginal discharge, higher level of pain on removal, and high proportion of women who would choose this therapy again or recommend it to others. In the same study, the authors reported on 1 patient who was labored with the pessary inadvertently left in situ until advanced stage of labor. She underwent a forceps-assisted vaginal delivery with loss of small ring-shaped part of her cervix due to thrombosis of a cervical vein, which was thought to be due to prolonged increased pressure and edema of the cervix that occurred during labor.[3]

Cervical Length Measurement With Pessary In Situ

Accurate transabdominal evaluation of the cervix is difficult, especially if the cervix is short. Transvaginal cervical length evaluation can also be challenging if the pessary is in place, as the standard transvaginal technique involves placement of the probe in the anterior fornix, which is difficult to achieve with the pessary in situ, and images are obscured due to shadowing from the pessary. Goya et al[25] reported a novel approach to evaluating cervical length with the pessary in situ. Adequate visualization of the cervix was achieved by passing the probe through the space between the pessary edge and posterior vaginal wall and inserting the probe just inside the pessary, touching the external cervical os. This approach requires guidance of the transducer initially posteriorly to pass the edge of the pessary, and then angle anteriorly once inside the pessary. The patients in the study tolerated the technique well, with only 1 of 43 patients not able to tolerate the procedure due to discomfort.

Conclusions

In summary, the pessary is a promising therapy that is well-tolerated and potentially effective for prevention of spontaneous preterm birth and treatment of cervical insufficiency. Further studies are necessary to delineate the role of pessary treatment either as a primary or an adjunct therapy in certain clinical scenarios.

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