FULL TEXT ARTICLE

Cervical pessary to prevent preterm birth in women with twin gestation and sonographic short cervix: a multicenter randomized controlled trial (PECEP-Twins)

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Introduction

Spontaneous preterm birth (SPB) is a major risk factor for perinatal morbidity and mortality in twin gestations (more than half result in premature births). The frequency of twin gestations has increased over the years, from 19.8/1000 births in 1980 to 33.1/1000 births in 2012. [1] The increased risk for adverse outcomes in twin gestations is largely attributed to preterm birth and the rates in twins are 5-6 times higher. [2] A short cervix (<25 mm) is associated with early and very early preterm birth in twins, and 15% of women with twin gestations have a cervix ≤25 mm. [4] This measurement has become the method of choice for screening asymptomatic pregnant women at risk for preterm birth <24 weeks of gestation both in twin and singleton pregnancies; this is based on a systematic review and metaanalysis. [5]

Current options for the management of patients with a short cervix are: vaginal progesterone, [6] [7] [8] [9] cervical cerclage, [10] [11] and cervical pessary. [11] [12] A systematic review and metaanalysis showed that vaginal progesterone reduced the rate of preterm delivery in twins in cases of maternal short cervix by 30%, which was not statistically significant; however, a reduction was observed in the rate of neonatal morbidity [13] and confirmed recently. [14] Cervical cerclage has been reported to increase the frequency of adverse outcome in twin gestations. [15] [16] A cervical pessary to support the cervix in pregnant women with cervical insufficiency was introduced in 1960. Since then, several studies in pregnant women with cervical insufficiency have been published [17] [18] [19] [20] ; however, most were retrospective or

case-control. In the study by Arabin et al, [21] the use of the pessary in pregnant women with short cervical length (CL) on ultrasound reduced the risk of spontaneous birth, with a decrease being observed in the preterm birth rate in both singleton and twin pregnancies, in cases of maternal CL ≤25 mm.

A cervical pessary is a silicone ring with a smaller diameter to be fitted around the cervix and a larger diameter to fix the device against the pelvic floor. This effectively rotates the cervix toward the posterior vaginal wall and corrects the cervical angle. [22]

We designed a multicenter, randomized controlled trial to evaluate the effect of cervical pessary on the early SPB rate in asymptomatic women with a short cervix (CL ≤25 mm) carrying twins (PECEP-Twins Trial).

Materials and Methods

Trial design

A prospective, open-label, multicenter, randomized clinical trial was conducted in 5 hospitals in Spain. The ethics committees of all participating hospitals approved the protocol. The trial was registered as ClinicalTrials.gov (http://ClinicalTrials.gov) , number NCT01242410 (ctgov:NCT01242410) .

Participants

Women with twin pregnancies undergoing routine ultrasonography at 18-22 weeks of gestation were given the option of transvaginal ultrasonographic CL measurement as a predictor of SPB. [23] CL was measured according to the criteria of the Fetal Medicine Foundation. [24] Despite large variations in gestational age at measurement, cut-off point for CL, and definition of preterm birth among countries, second-trimester CL is a strong predictor of preterm birth in women with a multiple pregnancy. [25] Women with a CL ≤25 mm were invited to participate in the PECEP-Twins Trial. Exclusion criteria were major fetal abnormalities, painful regular uterine contractions, active vaginal bleeding, ruptured membranes, placenta previa, and history of cone biopsy or cervical cerclage in situ. Gestational age was determined from menstrual history and confirmed by measurement of fetal crown-rump length at a first-trimester scan carried out routinely at all participating hospitals. Recruitment began in January 2011 and was extended to July 2014.

Quality control of screening, handling of data, and verification of adherence to protocols at the different centers were performed on a regular basis by trial coordinators. Obstetricians who performed the scans had received extensive training and passed a practical examination administered by an expert to demonstrate their competence in cervical assessment. All

images of the cases included in the trial and all cases of preterm birth were reviewed and discussed centrally. The central team in turn instructed the other centers in the use of the pessary.

Randomization and masking

After providing written informed consent, women were randomly allocated to cervical pessary insertion or expectant management at a 1:1 ratio. The randomization sequence was computer generated with variable blocks of 2 and 4, stratified for center and parity. The random-number lists were created by the Statistics Unit of the Vall d'Hebron Hospital Research Institute and implemented by the use of a central telephone. The allocation code was disclosed after the patient's initials had been confirmed. The randomization sequence was not accessible to the investigators or the trial coordinator. Outcome assessors were blinded to the interventions. This study was open label since masking to intervention was not possible.

Interventions

Cervical and vaginal swabs were taken in all patients for Gram stain microbiologic studies (culture for trichomoniasis, *Candida* , group B streptococcus, and bacterial vaginosis). If clinical symptoms of infection were detected, empiric treatment according to our hospital protocol and Spanish Obstetrician and Gynecologist Society was provided and pessary insertion delayed by 1 week. [26] Vaginal examination with a speculum was performed to observe cervical dilatation or visible membranes. Patients allocated to the pessary group had one inserted and were given detailed instructions on its subsequent management. Special emphasis was placed on the need to immediately report any adverse symptoms. Correct placement of the pessary was determined by transvaginal ultrasound and CL was measured. In women with a cervical pessary, sonographic visualization of CL is difficult owing to the shadow cast by the silicone on the cervix. We found that good visualization of the cervix is enabled by passing through the virtual space between the pessary and posterior vaginal wall and inserting the probe inside the pessary, which, if possible, touches on the external cervical os or anterior cervical lip. We propose this new technique for measuring and monitoring CL in women with a cervical pessary. [27]

All these interventions were performed on the same day. The pessary was not removed when symptoms of infection occurred after pessary insertion; however, appropriate antibiotic (clindamycin) therapy was given.

EC-certified cervical pessaries for the indication of preventing SPB (CE0482/EN ISO 13485: 2003 Annexe/III of the Council Directive 93/42 EEC) were employed. A one-size pessary was used following the recommendations of Dr Arabin GmbH and Co KG: 65 × 25 × 32 mm

(lower larger diameter, height, and inner diameter) purchased from Dr Arabin GmbH and Co KG; only in patients who had problems with the pessary did we consider changing the size of the pessary.

Both groups were seen every month until delivery. The following procedures were carried out: (1) transabdominal ultrasound for fetal biometry and assessment of fetal well-being; (2) maternal satisfaction questionnaire regarding pessary placement in the pessary group; (3) vaginal swab taken for study of Gram stain and microbiology (culture for trichomoniasis, *Candida* , group B streptococcus, and bacterial vaginosis); and (4) transvaginal ultrasound for CL measurement.

The pessary was removed during the 37th week of gestation. Indications for pessary removal <37th week were active vaginal bleeding, an episode of preterm labor with persistent contractions despite tocolysis (>5 contractions every 30 minutes, without reduction or end with tocolytic drug), or severe patient discomfort.

Preterm labor was defined as uterine contractions detected and CL shortening according to gestational age; in these cases, tocolysis and corticosteroids were administered. Atosiban was the first-line tocolytic owing to the twin nature of the pregnancy.

Patients whose pessary was removed (even on the day of insertion) remained in the trial (intention-to-treat analysis). The pessary was not initially removed if preterm rupture of membranes occurred: these patients were followed up at the hospital and, if labor began or chorioamnionitis was detected, the pessary was removed. Sexual intercourse was not prohibited in either groups.

Outcome measures

The primary outcome was SPB <34 weeks (238 days) of gestation. Secondary outcomes were: birthweight, intrauterine fetal demise, neonatal death, neonatal morbidity (intraventricular hemorrhage, respiratory distress syndrome, retinopathy of prematurity, necrotizing enterocolitis, proven or suspected sepsis, need for neonatal special care [neonatal intensive care unit, need for ventilation, phototherapy, antibiotics, or blood transfusion]), composite adverse outcomes (intraventricular hemorrhage, respiratory distress syndrome, retinopathy of prematurity, necrotizing enterocolitis, and proven or suspected sepsis), significant maternal adverse effects (heavy bleeding, cervical tear, uterine rupture, intolerance to pessary), SPB <37 weeks, SPB <28 weeks, spontaneous rupture of membranes <34 weeks, chorioamnionitis, hospitalization for threatened preterm labor <34 weeks (mean duration of hospital stay, use of tocolytic treatment type of tocolytic, days of treatment, dose) and incidence of vaginal infections. Placentas were analyzed in both groups. Chorioamnionitis was defined as acute inflammation of the extraplacental membranes, chorion, and amnion, by pathologic study after delivery. [28]

Data analysis

Sample-size calculation was based on a reduction in the frequency of spontaneous delivery <34 weeks, from 50% in the expectant management group to 25% in the pessary group, with power of 80%. To detect this difference at a significance level of 5%, we needed to recruit 126 patients with CL of ≤25 mm.

Analysis was performed according to the intention-to-treat principle. The means and SD summarized baseline data for the pessary and expectant management groups (Table 1 (tbl1)). Comparisons between groups were made with the Mann-Whitney *U* test. Neonatal outcomes were analyzed as nonindependent data if they occurred in the same birth. Univariate comparisons of dichotomous data were made with Fisher exact test. *P* values for all hypotheses were 2-sided, and *P* values <.05 were considered statistically significant. The risk of SPB <34 weeks was quantified by the relative risk (RR) and 95% confidence interval (CI). Multivariate analysis was performed by logistic regression. [29] The interval from randomization (pessary or not) to delivery was assessed using Kaplan-Meier analysis, [30] where gestational age was the time scale, spontaneous delivery was the event, and elective deliveries were treated as censored. For purposes of this analysis, all pregnancies were considered to be no longer at risk at the start of the 34th week. All statistical analyses were performed with a software package (SPSS, Version 16; IBM Corp, Armonk, NY). No interim analysis was planned for this trial.

Table 1

Characteristics of study participants

Baseline characteristics of the study subjects [a] (tbl1fna)	Pessary (n=68)	No treatment (n=66)
Maternal Age (years)	35.4 (3.6)	35.9 (5.6)
Body mass index [b] (tbl1fnb)	24.3 (1.5)	24.7 (2.0)
Obstetric history — no. (%)		
Nulliparous	31 (45.6%)	29 (43.9%)
Parous with no previous preterm births	26 (36.4%)	25 (36.8%)
Parous with ≥ 1 previous preterm births	11 (16.7%)	12 (17.6%)
Cigarette smoking during pregnancy — no. (%)	10 (14.7%)	9 (13.6%)
Race — no. (%) [c] (tbl1fnc)		
White European	38 (57.6%)	41 (60.3%)

Baseline characteristics of the study subjects [a] (tbl1fna)	Pessary (n=68)	No treatment (n=66)
Latin American	16 (24.2%)	15 (22.1%)
Others	12 (18.2%)	12 (17.6%)
Gestational age at randomization (weeks)	22.1 (0.8)	22.5 (0.7)
Cervical length at randomization (mm)	19·2 (3.5)	19.6 (3.6)
Funnelling at randomization (yes)	7 (10.3%)	8 (12.1%)
Sludge at randomization (yes)	1 (1.4)	1 (1.5%)
Pregnancy after ART	21 (30.9%)	20 (30.3%)
Monochorionic Twins	13 (19.1%)	12 (17.6%)

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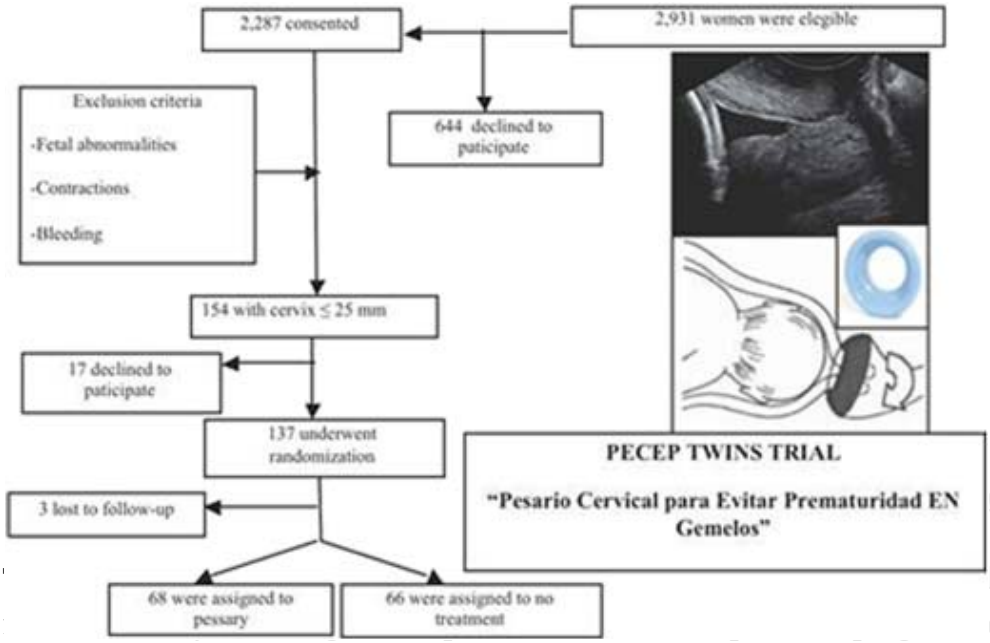
a Plus-minus values are means. p >0.05 for all between-group comparisons

b Body mass index: weight in kilograms divided by the square of height in meters

c Race was self-reported.

Results

The PECEP-Twins Trial was conducted from January 2011 through July 2014. The trial was planned to start in June 2008; however, funding became available in 2011. During the study period, 2931 women with twin pregnancies were invited to undergo transvaginal ultrasonographic CL measurement during the second-trimester scan (18-22 weeks of gestation); 2287 gave their written informed consent to participate. Median CL was 31 mm (range 8-54 mm) and length ≤25 mm was detected in 154 of the women (6.7%). In all, 137 women with short cervix (88.9%) agreed to participate in the trial. Pregnant women in this group were randomly assigned to be treated with a pessary or expectant management (Figure 1 (fig1)). Three patients were lost to follow-up: 2 in the pessary group and 1 in the expectant management group.



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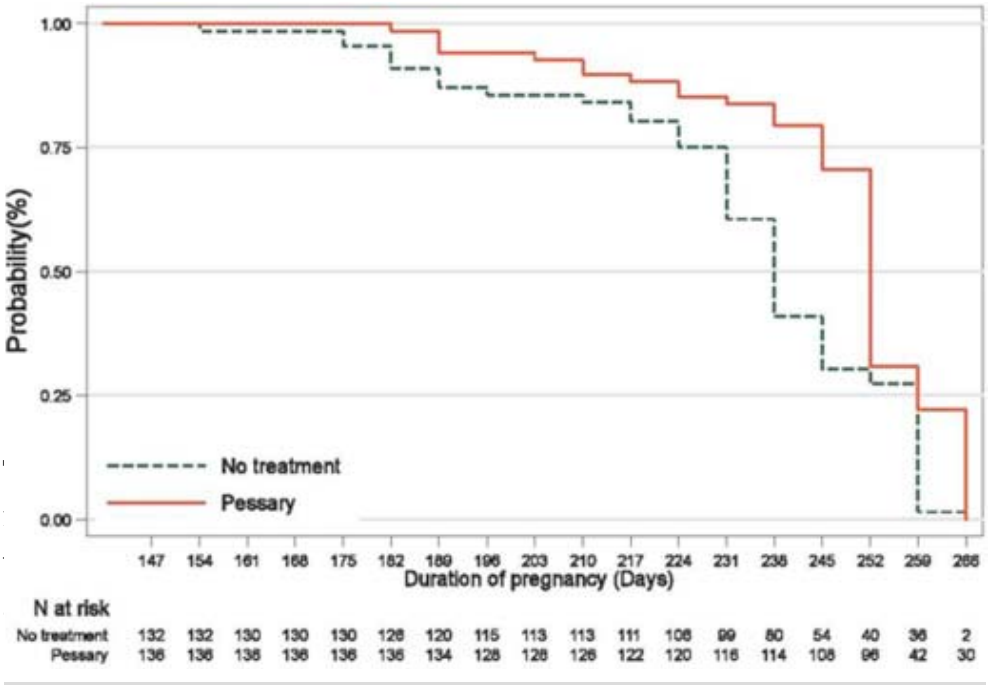
y mass index, es, and gestational age at the time of randomization) (Table 1 (tbl1)). No cervical dilatation or visible membranes were observed in this group of patients. A third of pregnancies in both groups resulted from assisted reproductive techniques and approximately 20% of both groups were monochorionic twins (Table 1 (tbl1)).

The primary outcome rate–spontaneous birth <34 weeks of gestation–was 16.2% (11/68) in the pessary group and 39.4% (26/66) in the expectant management group (RR, 0.41; 95% CI, 0.22–0.76; *P* = .003). Seven women (4 in the pessary group and 3 in the expectant group) had medically indicated preterm deliveries (1 case in each group <34 weeks). The interval from randomization (pessary or not) to delivery was assessed using Kaplan-Meier analysis (Figure 2 (fig2)). The cumulative percentage of patients who did not give birth spontaneously <34 weeks was significantly higher in the pessary group than in the expectant management group (hazard ratio, 0.50; 95% CI, 0.41–0.62; *P* = .0002). The risk of SPB <34 weeks of gestation did not vary significantly with regard to maternal age, body mass index, race, obstetric history, or CL at the time of randomization.



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29/66, 43.9%) than
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expectant management group (31/66, 46.9%) than the pessary group (25/68, 36.7%) (RR, 0.78; 95% CI, 0.52–1.17). However, these differences were not statistically significant (Table 2 (tbl2)).

Table 2

Outcomes according to treatment group

Pregnancy outcome	Pessary (n = 68), no. (range/%)	No treatment (n = 66), no. (range/%)	*P* value	RR (CI 95%)
Spontaneous delivery at <28 wk	4 (5.9)	9 (13.6)	ns	0.43 (0.14–1.33)
Spontaneous delivery at <34 wk	11 (16.2)	26 (39.4)	.003	0.41 (0.22–0.76)
Any delivery at <34 wk	12 (17.6)	27 (40.9)	.002	0.43 (0.24–0.78)
SPB for monochorionic twins	23.0	50.0	.01	
Spontaneous delivery at <37 wk	47 (69.1)	48 (72.7)	ns	0.95 (0.76–1.18)
Gestational age at delivery, wk	35.3 (2.9)	33.1 (3.9)	.01	

Pregnancy outcome	Pessary (n = 68), no. (range/%)	No treatment (n = 66), no. (range/%)	*P* value	RR (CI 95%)
Days admitted for threatened preterm delivery	3.5 (2–5)	3.9 (2–6)		
Tocolytic therapy	22 (32.3)	29 (43.9)	ns	0.74 (0.47–1.14)
Corticosteroid treatment for fetal maturation	25 (36.7)	31 (46.9)	ns	0.78 (0.52–1.17)
Chorioamnionitis	2 (3.0)	2 (2.9)	ns	0.97 (0.14–6.70)
PPROM	1 (1.5)	6 (9.1)	ns	0.16 (0.20–1.31)
Cesarean delivery	29 (42.6)	28 (42.4)	ns	1.01 (0.68–1.49)
Vaginal delivery				
Spontaneous	20 (29.5)	21 (31.8)	ns	0.92 (0.55–1.54)
Instrumented	19 (27.9)	17 (25.8)	ns	1.08 (0.62–1.90)
Maternal side effects				
Vaginal discharge	68 (100)	35 (53.0)	.01	–
Pessary repositioning without removal	11 (16.2)	–		–
Pessary replacement	2 (2.9)	–		–
Pregnancy bleeding	3 (4.4)	3 (4.5)	ns	0.97 (0.20–4.64)
Cervical tear	0	0		–
Uterine rupture	0	0		–

Perinatal outcome	Pessary (n = 136), no. (%)	No treatment (n = 130), no. (%)	*P* value	RR (CI 95%)

Perinatal outcome	Pessary (n = 136), no. (%)	No treatment (n = 130), no. (%)	*P* value	RR (CI 95%)
Fetal death	0	2	ns	–
Neonatal death	0	0	ns	–
Birthweight <1500 g	13 (9.5)	17 (13.1)	ns	0.73 (0.37 –1.44)
Birthweight <2500 g	47 (34.6)	62 (47.7)	.01	0.72 (0.54 –0.97)
Adverse outcomes				
Necrotizing enterocolitis	0	2 (1.5)	ns	–
Intraventricular hemorrhage [a](tbl2fna)	0	4 (3.0)	ns	–
Respiratory distress syndrome	8 (5.9)	8 (6.1)	ns	0.96 (0.37 –2.47)
Retinopathy	0	0	ns	–
Treatment for sepsis	4 (2.9)	6 (4.6)	ns	–
Composite adverse outcomes	8 (5.9)	12 (9.1)	ns	0.64 (0.27 –1.50)

CI , confidence interval; *ns* , not significant; *PPROM* , preterm prelabour rupture of membranes; *RR* , relative risk; *SPB* , spontaneous preterm birth.

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a Grade 2 in all infants.

No differences were observed in vaginal/cervical swab results, bacteria, and treatment. A positive vaginal and/or cervical swab was obtained in 6 of 68 patients in the pessary group (8.8%) and 7 of 66 in the expectant management group (10.6%). The most frequent microorganism was *Mycoplasma hominis* in both groups (3/6 [50%] in the pessary group and 4/7 [57.1%] in the expectant management group). Erythromycin was the most frequent antibiotic used in both groups (3/68 [4.4%] of the pessary group and 4/66 [6.1%] of the expectant management group).

Pessary was associated with a significant reduction in the rate of birthweight <2500 g (*P* = .01; RR, 0.72; 95% CI, 0.54–0.97). No differences were observed in other secondary outcomes between groups concerning neonatal morbidity and neonatal mortality (Table 2 (tbl2)).

No differences between groups were observed in relation to the number of patients followed up for intrauterine growth restriction prenatally (3/68 [4.4%] in the pessary group vs 2/66 [3.0%] in the expectant management group). In addition, no differences were observed in terms of histologic chorioamnionitis, induced delivery rate, or premature preterm rupture of membranes in the expectant management group (Table 2 (tbl2)). No major maternal adverse events occurred concerning pessary use (Table 2 (tbl2)). However, the following side effects occurred in the pessary group: all pregnant women with a pessary had vaginal discharge after placement of the pessary (68/68), and 11 (16.2%) patients with a pessary required pessary repositioning without removal. Two (2.9%) required removal and replacement of the pessary. Results of the maternal satisfaction questionnaire were as follows: pain during pessary insertion, 4 (scale 0-10); pain during removal, 7 (scale 0-10), and recommendation of this intervention to others, 63/68 (95.0%). No changes in the size of the pessary were needed. The placement of a cervical pessary was associated with a significantly higher rate of vaginal discharge (100% vs 53%) (*P* = .0001).

Data on pregnancy outcome were also obtained from 2205 (96.4%) of 2287 women in whom CL had originally been measured; 44 (28.6%; 11 in the pessary group, 26 in the expectant management group, and 7 declined to participate) of 154 women with CL ≤25 mm and 206 (10.1%) of 2051 with CL >25 mm delivered preterm.

Comment

Main findings

The finding of the study demonstrates that in selected twin pregnancies (mothers with short cervix), placement of a cervical pessary at 22 weeks of gestation reduces the SPB rate at 34 weeks of gestation. In our expectant management group, the SPB rate <34th week was 39.4%; however, in our pessary group, this rate was reduced to 16.2%. Also, a reduction in the rate of birthweight <2500 g was observed in the pessary group; no differences were observed in the rate of adverse neonatal outcomes between the groups. Although there was a significant reduction in the rate on SPT, we did not find a significant reduction in neonatal morbidity. The reason for this is unclear. It is possible that a larger sample may be necessary to demonstrate such a finding; the trial was not designed with sufficient power to address these end points. Considering the prolongation of pregnancy and the reduction in low birthweight in twins, the cervical pessary should be view as an intervention for this high-risk group.

Consequently, our study was supported by the strength of recruiting nearly 3000 twin pregnancies following a mid-trimester anomaly scan. These patients were requested to consent to a CL assessment, permitting us to detect a large number (approximately 6% of this large population) of women at increased risk of preterm birth. The women who agreed to participate were randomized centrally at the Vall d'Hebron Hospital, and the follow-up and pessary insertion techniques were thoroughly controlled. Using this model conferred significance on our findings since, although more patients were included in our study, the results matched those of previous research: a low rate of preterm birth (<34 weeks, <20%) in the pessary group compared to 39% in the expectant management group. No statistical differences were observed in the preterm birth rate at <28 weeks between the 2 groups, probably because the pessary mechanism cannot modify a very short cervix (delivery occurred in the group of shorter cervix); no statistical differences were observed in the preterm birth rate at <37 weeks; one reason could be the overdistension of twins and the impossibility of a pessary maintaining a long cervix >37 weeks.

Strengths and limitations

The strengths of the study are: (1) randomized controlled trial in one country; (2) selected twins by CL and no changes to the protocol after commencement of the trial; (3) measurement of CL by appropriately trained sonographers; (4) patient follow-up by the same physicians who randomized patients, experts in pessary management during pregnancy; and (5) the SPB rate <34 weeks was the same as estimated for the power calculations.

Long-term follow-up of the infants was planned to detect possible developmental impairments and compare them between the 2 study groups.

CL assessment, as a screening test, is used because of its relatively low cost, short learning curve, and tolerability for patients. [6] In addition, the pessary is an economical, noninvasive procedure and is easy to insert and remove when required [22] ; also, we previously described a new technique for monitoring CL in pregnant women with a pessary. [27] However, it should be pointed out that when pessaries are used, patients will have a moderate increase in a white, inodorous, vaginal discharge. Furthermore, a proportion of these patients (15% in our group) reported feeling the pessary inside the vagina after weeks without symptoms. For this reason, patients should be advised to see their doctor if any abnormal symptom such as feeling the pessary appears. Only 2 cases of pessary withdrawal were reported in the entire group and tolerability was not an issue, even in this particular case. As the satisfaction questionnaire showed, patients had more pain during pessary removal than insertion; however, a majority would recommend this intervention to others. It is also remarkable that no severe bleeding was reported in the pessary group compared to the expectant management group.

The proposed mechanism of action of a cervical pessary remains to be determined. Theoretically, the potential effect relies on their mechanical ability to bend the cervix backward, not only slightly elongating it but also changing the uterocervical angle, which not only adds some strength to the cervical canal but also diminishes the contact of intact membranes with the vaginal medium, in some way preserving its integrity. [22]

Although masking is not possible owing to the nature of the intervention, use of the pessary might have affected medical decision-making. We believe that the nonmasked nature of this trial did not cause substantial bias since the management and treatment, if necessary, were similar for the 2 groups, as described in “Materials and Methods” and “Results.”

Comparison with results of previous studies

Cervical pessary in nonselected twin gestations has not reduced the frequency of preterm birth in a study. [31] [32] The frequency of preterm birth in twin gestations did not differ in women allocated to pessary vs no pessary. However, Liem et al [31] reported a preterm birth rate <34 weeks of 14% when using a pessary for CL <38 mm at 22 weeks compared to nearly 30% in a matched short CL control group. Despite the limitation of CL (25th percentile, between 26-38 mm in a twin gestation is not a short cervix), the results were sufficiently promising to warrant further study. The second randomized controlled trial in unselected twins could not confirm these results. [32] In this study, the cervical pessary was removed at <34 weeks in 22.3% of pregnancies; however, they did not report the week (or range) and gestational age at delivery in this group of patients. It would also be of interest to know the percentage of patients with short cervix in this group. If it was high and the pessary was removed soon after insertion, it may explain the differences between these results and those of another twin pregnancy and pessary study published earlier. [31] In a previous study by our group on pessary use for preventing preterm birth in singleton pregnancies, the authors did not remove the pessary for preterm prelabor rupture of membranes, and no differences were detected regarding chorioamnionitis or neonatal sepsis between groups. [14] A potential limitation of the study, as described by the authors in the article, is that many research team doctors were involved in pessary insertion; however, unlike with CL measurement, they did not receive any supervised training in the procedure. They report a case of cervical edema associated with a pessary requiring removal under general anesthesia. This may have been a case with uterine contractions that were not diagnosed rapidly. During the follow-up of these patients with cervical pessary, it is important to question the patient about pain and evaluate CL with ultrasound to detect any cervical shortening since early detection and treatment of threatened preterm labor are paramount. [21] [22] Perhaps it would be of interest to consider establishing a training program for pessary insertion and follow-up of these patients. The authors also reported the use of vaginal progesterone in 2 patients of the control group; in

both cases, gestational age at delivery was >34 weeks. Some recent studies showed that progesterone could improve results in twin pregnancies (preterm birth rate and morbidity). [6] [7]

Conclusions and implications

Cervical pessary could have potential value as a treatment for a high risk of SPB, could be beneficial in pregnant women with a short cervix carrying twins regardless of their obstetric history, and may reduce the risk of SPB in nulliparous women. In conclusion, the pessary is an affordable, is a safe, and may be a reliable alternative for preventing SPB in a population of appropriately selected at-risk twin pregnancies previously screened by CL assessment at the mid-trimester scan.

References

1. Hamilton B.E., Martin J.A., and Ventura S.J.: Births: preliminary data for 2012. Natl Vital Stat Rep 2013; 62: pp. 1-20

2. Iams J.D., Romero R., Culhane J.F., et al: Primary, secondary, and tertiary interventions to reduce the morbidity and mortality of preterm birth. Lancet 2008; 371: pp. 164-175
Cross Ref (http://dx.doi.org/10.1016/S0140-6736(08)60108-7)

3. To M.S., Skentou C.A., Royston P., Yu C.K., and Nicolaides K.H.: Prediction of patient-specific risk of early preterm delivery using maternal history and sonographic measurement of cervical length: a population-based prospective study. Ultrasound Obstet Gynecol 2006; 27: pp. 362-367
Cross Ref (http://dx.doi.org/10.1002/uog.2773)

4. To M.S., Fonseca E.B., Molina F.S., Cacho A.M., and Nicolaides K.H.: Maternal characteristics and cervical length in the prediction of spontaneous early preterm delivery in twins. Am J Obstet Gynecol 2006; 194: pp. 1360-1365
Cross Ref (http://dx.doi.org/10.1016/j.ajog.2005.11.001)

5. Conde-Agudelo A., Romero R., Hassan S.S., and Yeo L.: Transvaginal sonographic cervical length for the prediction of spontaneous preterm birth in twin pregnancies: a systematic review and meta-analysis. Am J Obstet Gynecol 2010; 203: pp. 128.e1-128.e12
Cross Ref (http://dx.doi.org/10.1016/j.ajog.2010.02.064)

6. Romero R., Nicolaides K., Conde-Agudelo A., et al: Vaginal progesterone in women with an asymptomatic sonographic short cervix in the midtrimester decreases preterm delivery and neonatal morbidity: a systematic review and

metaanalysis of individual patient data. Am J Obstet Gynecol 2012; 206: pp. 124.e1-124.e19
Cross Ref (http://dx.doi.org/10.1016/j.ajog.2011.12.003)

7. Schuit E., Stock S., Rode L., et al: Effectiveness of progestogens to improve perinatal outcome in twin pregnancies: an individual participant data meta-analysis. BJOG 2015; 122: pp. 27-37
Cross Ref (http://dx.doi.org/10.1111/1471-0528.13032)

8. Fonseca E.B., Celik E., Parra M., Singh M., and Nicolaides K.H.: Fetal Medicine Foundation Second Trimester Screening Group. Progesterone and the risk of preterm birth among women with a short cervix. N Engl J Med 2007; 357: pp. 462-469
Cross Ref (http://dx.doi.org/10.1056/NEJMoa067815)

9. DeFranco E.A., O'Brien J.M., Adair C.D., et al: Vaginal progesterone is associated with a decrease in risk for early preterm birth and improved neonatal outcome in women with a short cervix: a secondary analysis from a randomized, double-blind, placebo-controlled trial. Ultrasound Obstet Gynecol 2007; 30: pp. 697-705
Cross Ref (http://dx.doi.org/10.1002/uog.5159)

10. O'Brien J.M., Defranco E.A., Adair C.D., et al: Progesterone Vaginal Gel Study Group. Effect of progesterone on cervical shortening in women at risk for preterm birth: secondary analysis from a multinational, randomized, double-blind, placebo-controlled trial. Ultrasound Obstet Gynecol 2009; 34: pp. 653-659
Cross Ref (http://dx.doi.org/10.1002/uog.7338)

11. Hassan S.S., Romero R., Vidyadhari D., et al: Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial. Ultrasound Obstet Gynecol 2011; 38: pp. 18-31
Cross Ref (http://dx.doi.org/10.1002/uog.9017)

12. Owen J., Hankins G., Iams J.D., et al: Multicenter randomized trial of cerclage for preterm birth prevention in high-risk women with shortened midtrimester cervical length. Am J Obstet Gynecol 2009; 201: pp. 375

13. Alfirevic Z., Owen J., Carreras Moratonas E., Sharp A.N., Szychowski J.M., and Goya M.: Vaginal progesterone, cerclage or cervical pessary for preventing preterm birth in asymptomatic singleton pregnant women with a history of preterm birth and a sonographic short cervix. Ultrasound Obstet Gynecol 2013; 41: pp. 146-151
Cross Ref (http://dx.doi.org/10.1002/uog.12300)

14. Goya M., Pratcorona L., Merced C., et al: Cervical pessary in pregnant women with a short cervix (PECEP): an open-label randomized controlled trial. Lancet 2012; 379: pp. 1800-1806
Cross Ref (http://dx.doi.org/10.1016/S0140-6736(12)60030-0)

15. Saccone G., Rust O., Althuisius S., Roman A., and Berghella V.: Cerclage for short cervix in twin pregnancies: systematic review and meta-analysis of randomized trials using individual patient-level data. Acta Obstet Gynecol Scand 2015; 94: pp. 352-358
Cross Ref (http://dx.doi.org/10.1111/aogs.12600)

16. Berghella V., Odibo A.O., To M.S., Rust O.A., and Althuisius S.M.: Cerclage for short cervix on ultrasonography: meta-analysis of trials using individual patient-level data. Obstet Gynecol 2005; 106: pp. 181-189
Cross Ref (http://dx.doi.org/10.1097/01.AOG.0000168435.17200.53)

17. Newcomer J.: Pessaries for the treatment of incompetent cervix and premature delivery. Obstet Gynecol Surv 2000; 55: pp. 443-448
Cross Ref (http://dx.doi.org/10.1097/00006254-200007000-00023)

18. Acharya G., Eschler B., Grønberg M., Hentemann M., Ottersen T., and Maltau J.M.: Noninvasive cerclage for the management of cervical incompetence: a prospective study. Arch Gynecol Obstet 2006; 273: pp. 283-287
Cross Ref (http://dx.doi.org/10.1007/s00404-005-0082-2)

19. Dharan V.B., and Ludmir J.: Alternative treatment for a short cervix: the cervical pessary. Semin Perinatol 2009; 33: pp. 338-342
Cross Ref (http://dx.doi.org/10.1053/j.semperi.2009.06.008)

20. Ting Y.H., Lao T.T., Wa Law L., et al: Arabin cerclage pessary in the management of cervical insufficiency. J Matern Fetal Neonatal Med 2012; 25: pp. 2693-2695
Cross Ref (http://dx.doi.org/10.3109/14767058.2012.712559)

21. Arabin B., Halbesma J.R., Vork F., Hubener M., and van Eyck J.: Is treatment with vaginal pessaries an option in patients with sonographically detected short cervix? J Perinat Med 2003; 31: pp. 122-133

22. Arabin B., and Alfirevic Z.: Cervical pessaries for prevention of spontaneous preterm birth: past, present and future. Ultrasound Obstet Gynecol 2013; 42: pp. 390-399

23. Crispi F., Llurba E., Pedrero E., et al: Gestational age-dependent normal values of ultrasonographic measurement of cervical length in the Spanish population. Prog Obstet Ginecol 2004; 47: pp. 264-271
Cross Ref (http://dx.doi.org/10.1016/S0304-5013(04)76002-1)

24. Honest H., Forbes C.A., Durée K.H., et al: Screening to prevent spontaneous preterm birth: systematic reviews of accuracy and effectiveness literature with economic modeling. Health Technol Assess 2009; 13: pp. 1-627

25. Lim A.C., Hegeman M.A., Huis In 'T Veld M.A., Opmeer B.C., Bruinse H.W., and Mol B.W.: Cervical length measurement for the prediction of preterm birth in multiple pregnancies: a systematic review and bivariate meta-analysis. Ultrasound Obstet Gynecol 2011; 38: pp. 10-17
Cross Ref (http://dx.doi.org/10.1002/uog.9013)

26. Cabero L., Llurba E., Goya M., Fabre E., Ruiz C., and Valls A.: Documentos de Consenso SEGO. http://www.prosego.com/categoria-guia-asistencia/medicina-perinatal/page/6/ (http://www.prosego.com/categoria-guia-asistencia/medicina-perinatal/page/6/)

27. Goya M., Pratcorona L., Higueras T., Perez-Hoyos S., Carreras E., and Cabero L.: Sonographic cervical length measurement in pregnant women with a cervical pessary. Ultrasound Obstet Gynecol 2011; 38: pp. 205-209
Cross Ref (http://dx.doi.org/10.1002/uog.8960)

28. Tita A.T., and Andrews W.W.: Diagnosis and management of clinical chorioamnionitis. Clin Perinatol 2010; 37: pp. 339-354
Cross Ref (http://dx.doi.org/10.1016/j.clp.2010.02.003)

29. Hosmer D.W., and Lemeshow S.: Applied logistic regression. New York: John Wiley, 2000.

30. Hosmer D.W.L.S.: Applied survival analysis: regression modeling of time to event data. New York: John Wiley, 1999.

31. Liem S., Schuit E., Hegeman M., et al: Cervical pessaries for prevention of preterm birth in women with a multiple pregnancy (ProTWIN): a multicenter, open-label randomized controlled trial. Lancet 2013; 382: pp. 1341-1349
Cross Ref (http://dx.doi.org/10.1016/S0140-6736(13)61408-7)

32. Nicolaides K.H., Syngelaki A., Poon L.C., et al: Cervical pessary placement for prevention of preterm birth in unselected twin pregnancies: a randomized controlled trial. Am J Obstet Gynecol 2016; 214: pp. 3-5