

# First Experience Using Brazilian Ingamed® Cervical Pessary in Twin Pregnancy: A Case Series

Janete Vettorazzi<sup>1,2,3,4\*</sup>, Cristiano Caetano Salazar<sup>3,4</sup>, Edimárlei Gonsales Valério<sup>1,2,3</sup>, Ana Lúcia Isotton<sup>4,5</sup>, Anthomy Petermann<sup>2</sup>, Marcos Wengrover Rosa<sup>1,4</sup>, Gabriela Francoes Rostirolla<sup>1,3</sup>

<sup>1</sup>Postgraduation Program in Health Sciences, Gynecology and Obstetrics, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brazil

<sup>2</sup>Department of Gynecology and Obstetrics, Medical School of UFRGS, Porto Alegre, Brazil

<sup>3</sup>Service of Gynecology and Obstetrics, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil

<sup>4</sup>Service of Obstetrics and Gynecology, Hospital Moinhos de Vento, Porto Alegre, Brazil

<sup>5</sup>Medicina Fetal Porto Alegre, Porto Alegre, Brazil

Email: \*jvettorazzi@hcpa.edu.br

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## Abstract

**Background:** The rate of prematurity in twin pregnancies is higher than 50%. Due to its multifactorial nature, different strategies are necessary to reduce the incidence of premature birth or to increase the gestational age at birth of pregnancies at risk. In this context, cervical pessary may be indicated in twin pregnancies with short cervix. **Methods:** In this case series, we describe six twin pregnancies that were considered as high-risk for preterm labor due to short cervix (CL < 30 mm) at second trimester and multiple risk factors for prematurity. Several strategies were associated for the goal of delaying gestational age at birth. The main strategies were: removal of labor activities, treatment of infections, vaginal micronized progesterone 400 mg/day and vaginal pessary insertion (Ingamed® Brazil). **Results:** The gestational age of insertion of the pessary ranged from 16 to 24 weeks. The gestational age of birth ranged from 26 to 34 weeks. Three of the pregnancies were delivered due to spontaneous onset of labor, and three were delivered due to medical reasons. The mean length of pregnancy since pessary insertion to birth was 9 weeks (range 2 to 17 weeks). All infants without severe fetal malformation were discharged from the hospital without major sequelae. **Conclusion:** The use of cervical pessaries associated to micronized progesterone at a dose of 400 mg/day may be an option in the management of twins at risk for preterm birth. More controlled studies are needed to evaluate the simultaneous use of cervical pessary and progesterone on twin pregnancies.

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## Keywords

Cervical Pessary, Ingamed Pessary, Progesterone, Twin Pregnancy, Preterm Birth

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## 1. Introduction

The number of twin births has increased in recent years [1]. About 50% of these are born before 37 weeks, which implies important fetal morbidity and mortality. As prematurity can be considered a multifactorial syndrome, preventive measures and management of cases at risk usually include actions related to the main contributing factors for preterm labor. One of the several factors which increase preterm birth is the presence of short cervix. Shortening of the cervical length (CL) is a predictor of preterm birth in singleton and twin pregnancies. The risk of preterm delivery is inversely related to cervical length (CL) assessed at 22 - 26 weeks of gestation, and a CL  $\leq$  25 mm is associated with 28% risk for birth before 28 weeks [2] [3]. The cut-off measure to classify a cervix as short in the second trimester is controversial for twin pregnancies. Different studies describe cut-off measures of 38 mm, 30 mm or 25 mm [2] [4] [5] [6]. In our clinical practice, a CL below 30 mm in twin pregnancies is considered as short. The cervical length is not routinely measured in Brazil's public health care system, and there is no national recommendation on this topic. Nevertheless, the medical staff responsible for the prenatal care of the patients described on this paper followed the International Society of Ultrasound in Obstetrics and Gynecology guidelines [7]. Currently, there are different strategies to manage twin pregnancies with short cervix (TPSC), most of them with no proven effectiveness. Cervical cerclage has been associated with increase in the frequency of adverse outcomes in twin pregnancies [8]. A systematic review and meta-analysis showed that vaginal progesterone reduced the rate of preterm delivery in TPSC [9] [10]. Likewise, a randomized study associated the use of cervical pessary in twin pregnancies of mothers with a short cervix with significant reduction of prematurity [9]. In other recent meta-analysis, intravaginal progesterone 400 mg/day was more effective than in the doses of 100 or 200 mg in cases of TPSC [11].

## 2. Patients and Methods

In this case series we describe six twin pregnancies that were considered as high-risk for preterm labor due to short cervix (CL < 30 mm) at second trimester. The patients were selected from one of the authors' private clinic (J.V.), after screening for short cervix on second trimester.

Cervical length was obtained between 20 and 24 weeks of pregnancy by transvaginal ultrasound, using a General Electric (GE) VOLUSON E8, with an endocavity transducer at a frequency of 7.5 MHz. Ultrasound was performed with the patient in a dorsal lithotomy position and with empty bladder. The cervix was

measured along its longitudinal axis. The cervix occupied approximately 50% - 75% of the image and pressure from the probe on the cervix was as little as possible. Cervical measurement was obtained by placing calipers at the external and internal OS, using a straight line between both of them. If the cervix was curved and the straight-line cervical length measurement was short, measurement obtained in two or more segments was performed to provide a more accurate estimation. The examination lasted from 3 to 5 minutes to detect possible changes in cervical length, and at least 3 measurements were obtained along that period.

The patients were managed on an individual basis. Some of them had multiple risk factors for prematurity, mostly previous infections. All patients had a cervical pessary (Ingamed® Brazil) inserted, received vaginal micronized progesterone at a dose of 400 mg/day and were removed from their work activities. The main baseline characteristics, CL, gestational age at pessary insertion and individual risk factors are described on **Table 1**.

### 3. Results and Discussion

The main maternal and fetal outcomes are described on **Table 1**. The mean CL and gestational age at pessary insertion were respectively 21 mm (range 10 - 28 mm) and 22 weeks (range 16 - 24 weeks). Mean age of delivery was 31 weeks

**Table 1.** Case series: Twin pregnant with short cervix.

	Case #1	Case #2	Case #3	Case #4	Case #5	Case #6
Maternal Age	36	39	33	38	41	41
Gravidity and parity	G2 P1*	G1	G1	G1	G2 P1*	G1A1
Cervical length (mm)	10	25	16	28	25	22
Cervical funneling	Yes (25 mm)	No	No	No	No	No
Amniotic fluid sludge	Yes	No	No	No	No	No
Chorionicity	Dichorionic, diamniotic	Dichorionic, diamniotic	Dichorionic, diamniotic	Monochorionic, diamniotic	Monochorionic, diamniotic	Monochorionic, diamniotic
Assisted reproduction procedure or ovulation induction	No	<i>In vitro</i> fertilisation	No	<i>In vitro</i> fertilisation	No	<i>In vitro</i> fertilisation
Risk factors	Bacterial vaginosis Urinary infection Bleeding in the first trimester Family stress and depression	Thrombophilia Anemia Hypothyroidism	Bacterial vaginosis Urinary infection Bleeding in the first trimester Family stress and depression	Cervical conization Thrombophilia Hypothyroidism	Family stress	Thrombophilia Urinary infection
Gestational age at cervical pessary insertion (completed weeks)	22	24	24	26	16	18

## Continued

Gestational age of birth (completed weeks)	29	34	26	34	33	28
Pregnancy Outcomes						
Gestational age at admission (completed 28 weeks)		32	24	28	32	25
Spontaneous labor	Yes	Yes	Yes	No****	No****	No****
Tocolytics	Atosiban	Atosiban, nifedipine	Atosiban	Nifedipine	No	No
GBS	Positive	Negative	Positive	Negative	Negative	Negative
Fetal evolution	Regular	Regular	Regular	AFD	FGR and marginal cord insertion	AFD, FGR
Others	Sludge empyrical treatment with clindamycin		Gestational diabetes control		Premature rupture membranes	
Neonatal Outcomes						
Birth weight (g)	1350 and 1253	2020 and 1826	680 and 750	1678 and 1470	1886 and 1970	686 and 916
5-minute Apgar scores	9 and 10	10 and 10	9 and 9	9 and 9	10 and 10	10 and 8
NICU stay (days)	70	31	17 and 142	47	23	89 and 66
Twin pair neonatal outcomes	Both discharged home without major sequelae	Both discharged home without major sequelae	Twin I: gastroschisis, fetal sepsis. Died after 17 days  Twin II: fetal sepsis. Discharged home without serious sequelae	Fetal sepsis. Both discharged home without major sequelae	Both discharged home without major sequelae	Twin I: fetal sepsis  Both discharged home without major sequelae

NICU: neonatal intensive care unit. GBS: Group B Streptococcal colonisation. \*Term delivery. \*\*Fetal growth restriction. \*\*\*Abnormal fetal Doppler. \*\*\*\*Delivey indicated by medical reasons.

(range 26 - 34), half of them due to spontaneous onset of labor. In three cases the decision to deliver was due to fetal conditions and not due to preterm labor: one because of non-reassuring well-being test and two because of intrauterine growth retardation associated to abnormal Doppler ultrasound. The mean length of pregnancy since pessary insertion to birth was 9 weeks (range 2 to 17 weeks).

All pregnancies were delivered by caesarean, and all patients received antenatal corticosteroids for fetal pulmonary maturation before delivery. Patients with a positive group B streptococcal colonisation test at the onset of preterm labor received antimicrobial prophylaxis. The neonatal mortality rate was 8%, and the newborns who deceased had important anatomical problems (gastroschisis).

The risk of spontaneous preterm birth increases significantly with the number of risk factors for prematurity [12]. In our group of patients, we observed that in the two cases where birth occurred before 28 weeks there were multiple factors related to prematurity such as polyhydramnios, hypothyroidism, first-trimester

bleeding, bacterial vaginosis, urinary tract infection, amniotic fluid sludge, cervical funneling and/or fetal malformations [13] [14] [15].

The prevention of premature birth should be carried out throughout the prenatal visits by screening all the possible associated conditions in order to provide proper and immediate treatment. The use of tocolytics, corticosteroids and antibiotic therapy may have contributed significantly to the success of the presented cases since, with the exception of fetuses with major malformations, all babies were discharged without serious sequelae.

#### 4. Conclusions

The prevention of prematurity in twins is challenging, and the association of different strategies is frequently used. Nevertheless, it still needs to be studied more deeply. In order to significantly reduce prematurity incidence, we consider the CL measurement of fundamental importance in all twin pregnancies [7] [16], as well as the use of progesterone at a dose of 400 mg/day in cases of short cervix [11].

Different authors assert that cervical pessary may be useful to reduce neonatal morbidity and mortality in the subgroup of women with TPSC without any serious adverse effects [5] [6]. Nevertheless, the pessaries used on this case series were manufactured by Ingamed® (“Ingamed-Materiais Médico Hospitalares” n.d.), which may differ from the Arabin® pessaries (“ARABIN® Cerclage Pessar Perforiert” n.d.) described on most studies [17] [18]. The Arabin® pessary is not easily available in Brazil, though. The lack of a control group without pessary insertion does not allow drawing any conclusion about its efficiency from this study, but it is important to highlight that this is the first publication utilizing the Ingamed® Brazilian pessary for preterm delivery prevention.

Considering the high morbidity and mortality associated to prematurity, especially when extreme, the reduction in the number of days of neonatal intensive care unit stay is important to reduce economic, family and social costs. Despite no official Brazilian recommendation for measurement of cervix in twin pregnancies, screening for asymptomatic cervical shortening in those patients seems to be necessary, once there probably are effective interventions that could be established. In this context, the pessary seems to be at least a safe measure to extend pregnancy length on selected TPSC.

#### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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