Design and Materials Influence on Clinical Functionality of the Cerclage Pessary Use in Prevention of Premature Birth

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The aim of this study is to present specific aspects related to the cerclage pessary use in the management of pregnant women at risk for premature birth and reveal the correlation that exists between implant surface and clinical functionality of these devices. In the clinical part of our study, we evaluated a group of 51 patients diagnosed by clinical and ultrasonography with shortened cervix, who received a cerclage pessary in order to prevent preterm delivery. According to gestational age, two groups were formed: group A (abortion) formed of 19 patients diagnosed with risk of abortion (gestational age < 23 weeks and 6 days) and group B (birth) formed of 32 patients diagnosed with risk of premature birth (gestational age > 24 weeks). We were interested in detecting adverse reactions and complications related to the use of cerclage pessaries and also to determine if this procedure is efficient in preventing premature birth. In addition to the clinical part of this study, we evaluated the mechanism of interaction of the cerclage pessaries with the fluids and the vaginal mucosa by analyzing the structure, design and surface of these devices. Cerclage pessaries are efficient in preventing premature birth. In order to decrease the number and severity of the adverse reaction related to the use of these intra-vaginal devices regular follow-up visits are indicated. Re-sterilization by ethylene oxide procedure of vaginal pessaries is prohibited because it severely modifies the surface of these apparatuses.

Keywords: cerclage pessary, preterm delivery, adverse reactions, polymeric surface

Cerclage pessary a non-invasive option of treatment of patients at risk of premature birth

Premature birth is as termination of pregnancy before 37 weeks [1]. Premature birth is a major public health problem due to the fact that it is the most important cause of neonatal mortality, most often before 32 weeks of gestation [1]. The etiology is multifactorial, but all causes have in common the dilation of the cervix. Although it is more common in patients with short cervix (<25 mm) and history of preterm birth some specialists demonstrated that premature birth can occur in women without risk factors [2].

Despite increasingly advanced and standardized treatments the rate of prematurity did not decreased over the last 40 years, but even continues to grow - the incidence in Europe varies between 5 to 9% [3, 4].

Considering that the risk of premature birth is inversely proportional to the length of the cervix, determining the exact dimension is a method of screening in patients before 24 weeks who are asymptomatic [5, 6].

After a complete examination, if a patient is at risk of preterm birth the following treatment solutions are available: tocolysis, insertion of a cerclage pessary or a classic cervical cerclage procedure [7-11]. The insertion of a cerclage vaginal pessary is a modern and non-invasive option of treatment.

Cerclage pessary use

Vaginal pessary is a device used in several pathologies such as urinary incontinence, uterine prolapse or premature birth.

Obstetrical completed by ultrasound examination and screening for common vaginal infections are mandatory prior to the insertion of a vaginal cerclage pessary [12-14]. The obstetrician will choose the appropriate type of cerclage pessary depending on the severity of the disease, urinary incontinence and sexual activity [10-14]. The efficiency of cervical cerclage by inserting a vaginal pessary in order to prevent preterm birth has been demonstrated in case-control studies [13, 14]. However cerclage vaginal pessary has not proven its effectiveness compared with other methods, if cervical length is greater than 25 mm [11]. It is less invasive compared with a cervical suture and its effectiveness in preventing premature birth has been shown in recent studies [15, 16]. Vaginal pessary cerclage can prevent internal cervical orifice opening of the cervix, which is often associated with separation of amnion and chorion, especially when the patient is standing [17]. Another advantage is that the pessary also prevents the elimination of the cervical mucus plug in the vagina [18].

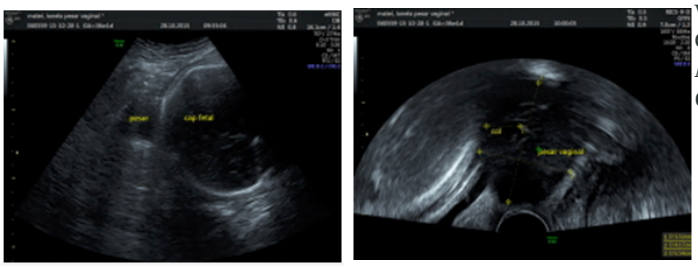

Fig. 1. Ultrasonographic aspect of a vaginal cerclage pessary - note the relation between the device and the internal orifice of the cervix

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All authors have participated equally in developing this study

Indications for cervical cerclage using a vaginal pessary

The cervical cerclage using a vaginal pessary is indicated to all pregnant patients between weeks 15 to 20 of pregnancy diagnosed with risk of abortion [12-14]. The device may be also used in patients diagnosed with risk of premature birth (> 24 weeks of gestation) but intact membranes [12-14]. The cerclage pessary does not enclose the cervix but it offers support and prevents further cervical disclosure [12-14].

Contraindications for cervical cerclage using a vaginal pessary

Vaginal infection is the main contraindication of vaginal pessary cerclage [12-14]. The device is also prohibited in patients with:

-premature ruptured membranes
-suspicion of chorioamnionitis
-ballooning of membranes outside the cervix
-at the onset/during labor
-congenital vaginal and uterine malformations
-cervical or vaginal cancer
-recent vaginal reconstructive procedures
-vesico-vaginal or recto-vaginal fistulas
-allergy to the substances in the composition of the pessary

Types of cerclage pessaries: design and materials aspects

Vaginal cerclage pessaries are made of flexible silicone, acryl, latex or plastic in order to be biologically inactive, non-carcinogenic and hypoallergenic [12-14]. The device has an annular shape. It circles the cervix and directs it toward the sacrum. Its shape resembles that of the vaginal fornix in order to surround the cervix as near as possible to the internal orifice of the cervix [12-14].

The vaginal cerclage pessary is disposable and can be stored at room temperature. It can be washed with soap and warm water but is not recommend to use disinfectant in order to clean it [12-14]. However, the cerclage pessary can undergo heat disinfection (temperatures up to 240 degrees Celsius) [12-14].

The distal portion part of the device is large (65-70 mm) and it remains in the vagina while the proximal portion is narrow (32-35 mm) and it must be positioned towards the cervix. The vaginal cerclage pessary is designed not only to support, but also to induce an oblique position of the cervix towards the sacrum [12-14].

The cerclage pessaries with a 32 mm proximal diameter are recommend to patients with less than 12 weeks of gestation or in second or third trimester of pregnancy if the cervix is greatly shortened [12-14].

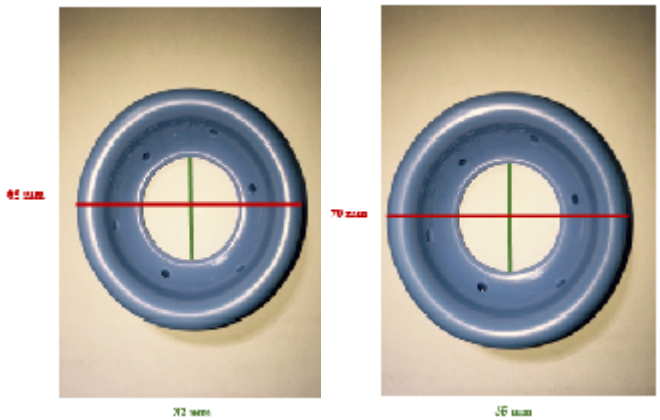

Fig. 2.Different types of cercalge pessaries (the diameters of the proximal and distal part vary according to patients features)

The cerclage pessaries with a 35 mm proximal diameter are recommend to patients with cervical edema or to those with a *V* opening of the internal cervical orifice (in order not to pressure on the membranes) [12-14].

The cerclage pessaries with a 65 mm distal diameter are recommend to short patients or primiparous patients, while in multiparous and high patients the devices with a distal diameter of 70 mm are indicated [12-14].

The height of the devices also varies. The 17-21 mm in height pessaries are suitable for singleton pregnancies, while the 25 mm devices are recommended for patients with important uterine distention (such as multiple pregnancy) [19, 20]. The 30 mm in height cerclage pessaries are indicated to pregnant women who associate uterine prolapse [20].

Functional aspects related to cerclage pessary use

The insertion and extraction of the device must be performed only be a healthcare professional [12-14]. The patient should empty her bladder before cerclage pessary fitting. Due to its elastic properties, the manipulation of the device does not require the use of anesthesia [15]. However a sterile gel may be used in order to the aid the discomfort during insertion [15].

The complications during the insertion of cerclage pessary such as iatrogenic rupture of membranes are very rare. However, complications such as vaginal erosion may occur if the patient does not attends follow up visits. During these examinations the obstetrician must extract the device in order to clean it. Screening for common vaginal infections is also mandatory due to the fact that the cerclage pessary predisposes to such contagions.

It is recommend to remove the vaginal pessary at 37 weeks if asymptomatic, or in case of uterine contractions and if premature rupture of membranes occurs in order to avoid ascending of bacteria [12-14].

Experimental part

Clinical study

The aim of this study is to present specific aspects related to the cerclage pessary use in the management of pregnant women at risk for premature birth and reveal the correlation that exists between implant surface and clinical functionality of these devices.

Material and methods

We performed a retrospective observational study (patient cohort) by evaluating a group of 51 pregnant women. The patients had between 15 weeks and 30 weeks of pregnancy and were diagnosed with risk of abortion (gestational age < 23 weeks and 6 days of pregnancy) or risk of preterm birth (gestational age > 24 weeks of pregnancy). All the patients included in this study have been admitted in the Department of Obstetrics and Gynaecology III of Bucharest University Emergency Hospital, between July 15 2014 and October 15 2015. A vaginal cerclage pessary was inserted as a method prevention of preterm delivery.

All the patients included in the study were first screened for genital infection - cultures were taken from the cervix and a microscopic examination of the vaginal secretion was also performed. Women with genital tract malformations, cervical scarring after surgery and congenital or acquired vaginal lesions were excluded.

The method of insertion is described below. We did not perform any type of anesthesia. Initially, the antisepsia of the vulvar region was executed using polyiodide. The vaginal device was greased using a sterile gel. The vaginal

pessary was initially inserted longitudinally and was orientated with the small diameter towards the cervix. Afterwards the device was ascended until the cervix was completely surrounded and was oriented towards the sacrum. The cerclage pessary must not cause discomfort; therefore each patient was asked to walk a few steps after insertion to determine if the device is correctly positioned. If the patient voiced any discomfort the cerclage pessary was changed.

After pessary insertion all pregnant women included in the study underwent a ultrasound examination in order to assess the fetal status and the position of the device in relation to the internal cervical orifice.

We analyzed the evolution of pregnancies for all the women included in the study and especially the infectious complications. All patients were assessed periodically (clinically, by ultrasound and paraclinically - genital sampling) - every three weeks. We were interested in detecting adverse reactions and complications related to the use of cerclage pessaries and also to determine if this procedure is efficient in preventing premature birth.

Scanning electron microscopy

In addition to the clinical part of this study we evaluated the mechanism of interaction of the cerclage pessaries with the fluids and the vaginal mucosa by analyzing the structure, design and surface of these devices.

Scanning electron microscope was used to evaluate 2 explanted cerclage pessaries from asymptomatic patients with 37 weeks of gestation. The same analysis was performed to a device that was extracted from a patient with severe vaginal erosion.

In order to determine the effect of re-sterilization on the polymeric component of the cerclage pessary we also analyzed a device that was explanted and disinfected by ethylene oxide procedure.

All the devices were investigated by SEM QUANTA INSPECT F (R=1.2 nm) equipped with FEG and EDAX, without any coatings.

Results and discussions

We included in the study 19 pregnant women with gestational age < 23 weeks and 6 days. The patients who were diagnosed with risk of abortion formed the group A (abortion). The remaining 32 patients with gestational age > 24 weeks diagnosed with risk of premature birth formed the B (birth) group (fig. 3). The clinical features of the patients pertaining to the two groups are presented in table 1.

Comparing the clinical characteristics of the patients enrolled in the two groups one can notice that the obstetrical outcomes are better when the cerclage pessary is inserted at a lower gestational age (table 1).

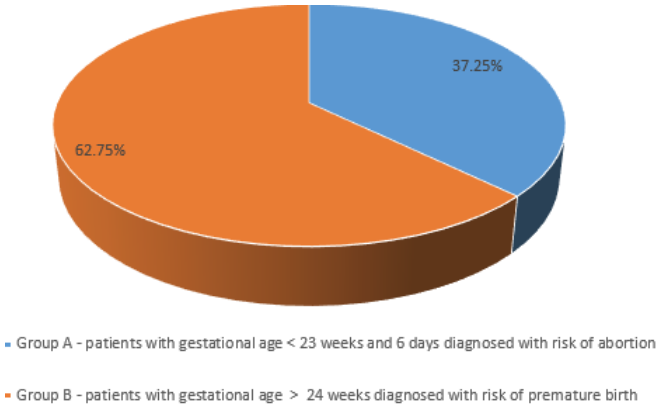

Fig. 3.The dividing of the studied patients according age to gestational

Within the analysed group of patients, we detected the following complications that can be related to the use of a cerclage pessary: local discomfort (n= 5 Group A - 1/ Group B - 4), genital infections (n=6 Group A -2/ Group B - 4), premature rupture of membranes (n=8 Group A - 3/ Group B - 5) and vaginal erosions (one patient pertaining to Group A (fig. 4).

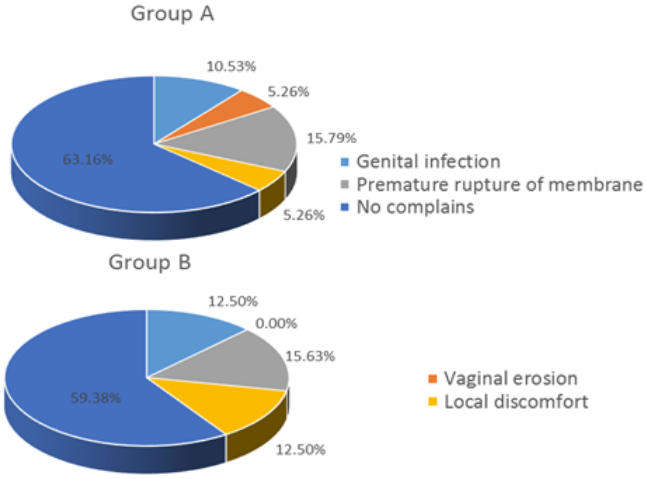

Fig. 4. The complications detected within the two analyzed groups of patients

Comparing the analyzed group with a group with similar demographic and obstetrical characteristics we did not notice statistically significant discrepancies regarding genital infections.

We have observed that there are no statistically significant differences between the two groups regarding the modality of delivery – the majority of patients included in this study delivered by Caesarean section (fig. 5).

Table 1

THE CLINICAL FEATURES OF THE PATIENTS INCLUDED IN THE STUDY

Group Chart Area	Maternal age (years)	Gestational age at insertion (weeks)	Cervical length at insertion (centimetres)	Cervical length at extraction (centimetres)	Gestational age at extraction (weeks)	Gestational age at birth (weeks)
Group A (median ± SD)	24.2 ± 3.2	19.6 ± 0.6	3.1 ± 0.3	2.1 ± 0.2	35.6 ± 0.6	36.1 ± 0.3
Group B (median ± SD)	26.1 ± 3.7	25.1 ± 0.5	2.6 ± 0.2	1.6 ± 0.2	33.1 ± 0.5	35.1 ± 0.2

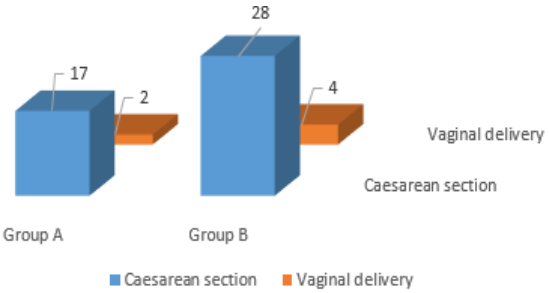

Fig. 5. The modality of delivery of the patients enrolled in the study

The surface analysis using scanning electron microscope highlighted different levels of degradation (fissures and cracks) of the polymeric component of the cerclage pessaries, proportional with the time spent inside the vagina. The surface analyzed in details by scanning electron microscope was the part that is more used of the pessary (the external part – that is in close contact with the vagina). It's important to mention that the interior part of the pessary didn't show any significant modifications.

We also detected numerous signs of degradation when analyzing the device that was extracted from the patient with vaginal erosion (fig. 6).

Based on the results shown in figure 7 one can observe that the sterilization by ethylene oxide didn't have a strong effect on the polymeric surface. The device that was explanted and disinfected by ethylene oxide procedure presented signs of severe degradation – numerous fissures and even cracks, which can predispose to severe adverse reactions (fig. 7).

In the clinical part of our study, we evaluated a group of 51 patients diagnosed by clinical and ultrasonography with shortened cervix, who received a cerclage pessary in order to prevent preterm delivery. According to gestational age two groups were formed: group A (abortion) formed of 19 patients diagnosed with risk of abortion (gestational age < 23 weeks and 6 days) and group B (birth) formed of 32 patients diagnosed with risk of premature birth (gestational age > 24 weeks). The length of the cervix was determined by trans-vaginal sonography – the mean cervical length during the insertion of the device was 3.1 cm in group A and 2.6 cm in group B. Although the universal trans-vaginal sonography screening for shorten cervix is debated we perform this procedure constantly and we always determine the exact cervical length prior to the insertion of cerclage pessary [16-22]. We also detected the cervical length prior to the extraction of the device – the mean value was 2.1 in group A and 1.6 in group B (table 1).

Analysing table 1 it can clearly be seen that the obstetrical outcomes are improved if the cerclage pessary is inserted at a lower gestational age (table 1). This aspect is very important because before 20 weeks of gestation the options of treating a patient with shorten cervix and history of preterm delivery are: surgical cerclage, insertion of cerclage pessary or the use of vaginal progesterone. Alfirevic *et al* demonstrated that there are no significant differences in rates of perinatal loss, neonatal morbidity or premature birth of these techniques [23]. However the advantage of using a cerclage pessary is that it can be used after an unsuccessful surgical cerclage [20]. Another advantage of using a cerclage pessary is that it can be inserted at a later gestational age [20]. In our study we enrolled 32 patients with gestational age > 24 weeks.

We were interested in detecting adverse reactions and complications related to the use of cerclage pessaries. 5 patients (1 from group A and 4 pertaining to group B) voiced local discomfort, especially during and in the first 24 h after the insertion of the device. This is a mild adverse reaction that may be decreased if the pessary is covered with antibacterial gel to provide lubrication for easier fitting [20]. Another rare complication raported during the insertion of a cerclage pessary is vaginal evisceration and the rupture of an enterocele [5]. We did not encountered these complications, probably because the patients with already demonstrated predisposing factors (e.g. – history of recent vaginal reconstructive and pelvic procedures and vaginal anomalies) were excluded [24-26].

One of the most frequent severe adverse reactions related to the use of cerclage pessaries is vaginal erosion that can even lead to vesico-vaginal or recto-vaginal fistula [2, 19, 27]. In our study we encountered one patient pertaining to group A with this adverse reaction. We were interested to determine if the surface of the cerclage pessary is modified. By surface analysis using scanning electron microscopy we detect significant alterations (multiple fissures and cracks in the polymeric surface – fig. 7) [28, 29]. These cracks, located on the exterior part of the pessary are the reason for the apparition of the vaginal erosion, because the vaginal mucosa is close contact with

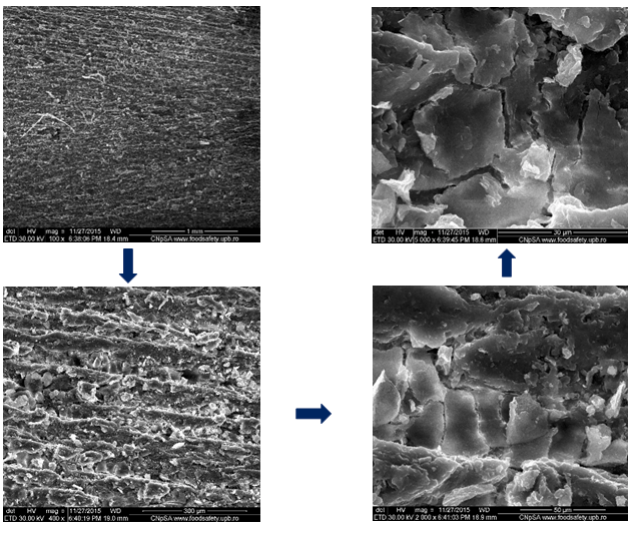

Fig. 6. SEM images showing the surface analysis of the cerclage pessary extracted from a patient with vaginal erosion – note the presence of some organic deposits and multiple fissures and cracks in the polymeric surface

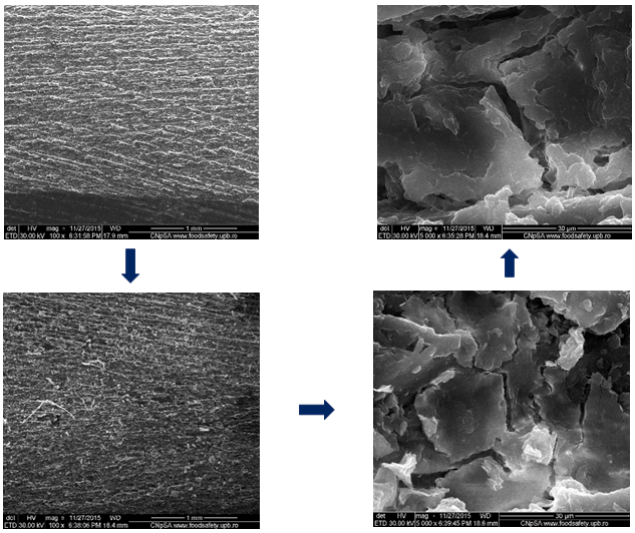

Fig. 7. SEM images showing the surface analysis of cerclage pessary was re-sterilized using the ethylene oxide procedure– note the presence of numerous fissures and cracks in the polymeric surface

the modified polymeric surface of the device. It seems that vaginal erosion develops in patients with neglected vaginal pessaries, however our patient attended periodic visits and had no genital infections [2].

The predisposition to genital infections is one of the most debated adverse reactions that have been related to the use of cerclage pessaries. In our study, a genital infection was documented in 6 patients. It has been already demonstrated that the intra-vaginal device predisposes to bacterial colonization and pelvic infection, that determines spontaneous rupture of membranes and uterine contractions leading to preterm delivery [12, 14, 20]. However regular follow-up visits can decrease the risk be rapid initiation of treatment [12, 14, 20, 30]. This is why all patients enrolled in our study were assessed periodically (clinically, by ultrasound and paraclinically - genital sampling).

Since the manufacturer does not provide enough data about how to clean and disinfect the cerclage pessary we analyzed the effect of re-sterilization by ethylene oxide procedure on the polymeric component of the device. The investigations performed using scanning electron microscope highlighted signs of severe degradation (fissures and even cracks) which can predispose to severe adverse reactions.

Analysing figure 6 and figure 7 one can observe a very important wear pattern of the polymeric surface that was observed in all the cases of retrieved pessaries – note the presence of numerous cracks and organic deposist even on the re-sterilized device.

Based on this analysis and our clinical experience, we recommend the use of the sterile gel after the cleaning of the pessary during the maintenance of these types of devices. Also, the modification of the polymeric surfaces using different surface treatment like plasma treatment could conduct to a better clinical performance of these devices because the wear will be reduced.

Conclusions

Cerclage pessaries are efficient in preventing premature birth. In order to decrease the number and severity of the adverse reaction related to the use of these intra-vaginal devices regular follow-up visits are indicated. Re-sterilization by ethylene oxide procedure of vaginal pessaries is prohibited because it severely modifies the surface of these apparatuses.

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