https://doi.org/10.5272/jimab.2025311.6029

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

Journal of IMAB. 2025 Jan-Mar;31(1)

Review article

STRATIFICATION OF GRAVID CERVIX SUSPENSION – A REVIEW

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ABSTRACT

Cerclage, ARABIN pessary (AP) and progesterone demonstrate stratification of invasive, mini-invasive drug-induced suspension of the gravid cervix, manage the isthmico-cervical incompetence and regulate the rate of late abortions and preterm delivery (PTD).

In singleton pregnancies, the lowest PTD rates are as follows: for AP combined with cerclage and vaginal progesterone - 44.4%, PTD <37 g.w.; for long-term tocolysis - 30.8%, PTD <36 g.w.; for transabdominal cerclage - 8%, PTD <32 g.w. For cerclage alone, the lowest PTD rate <34 g.w. is 32.4%, for cerclage with AP - 27.7%, and for cerclage with vaginal progesterone - 17%. For indicated AP, PTD is 16%, and for electively inserted one, it is 9.4%. For AP combined with vaginal progesterone, the value is 4.6%, and for vaginal progesterone alone it is 4%. In this review, the lowest PTD rate <34 g.w. reported for AP used alone in multiple pregnancies is 18.4%.

ARABIN pessary is superior or non-inferior to cerclage in incompetent cervix in singleton pregnancies because of the similarity in PTD results; however, there is evidence that its effectiveness prevails over vaginal progesterone in twin pregnancies where a non-active approach is preferred. ARABIN cerclage pessary combined with vaginal progesterone destabilizes the non-significantly prevailing effectiveness of vaginal progesterone administered alone in singleton pregnancy. AP is not included in the guidelines as a standard treatment, although research findings suggest it is likely to be implemented as a principal recommendation in the future for gravid cervix suspension, either in combination or alone.

Keywords: ARABIN pessary, cerclage, cervical incompetence, preterm delivery, progesterone, gravid cervix suspension,

BACKGROUND

Cerclage, ARABIN pessary (AP) and progesterone demonstrate stratification of invasive, mini-invasive and drug-induced suspension of the gravid cervix, manage the isthmico-cervical incompetence and regulate the rate of late abortions and preterm delivery (PTD) [1, 2, 3, 4, 5, 6, 7, 8].

Cervical incompetence (CI) is one of the most important causes of late abortion and PTD. It consists of the inability of the gravid cervix to retain the conceptus due to painless progressive dilation without uterine contractions or with contractions insufficient to explain the cervical changes, with subsequent vaginal protrusion or spontaneous preterm premature rupture of the membranes (PPROM), intra-amniotic microbial invasion or PTD, most frequently under conditions of congenital or acquired structural and functional cervical defects. There is an increased risk, and CI is suspected in cases of short cervical length (CL) ≤25 mm, <24 g.w., or < 28-32 g.w., V or U-shaped funneling and dilated internal os over 10 mm. Transvaginal ultrasound (TVU) at the beginning of the midtrimester is useful in detecting asymptomatic pregnant women, those at high risk for PTD or with suspected CI [1, 4, 6, 7, 9, 10, 11, 12].

Cervical incompetence is likely to be a form of collagenopathy or may result from intra-amniotic infection, previous uterine or cervical intervention and other clinical situations, such as decidual haemorrhage, uterine overstretching or disturbance in maternal-fetal tolerance. The clinical course of CI consists of single or recurrent losses, ≥2 in midtrimester, or PTD <28 g.w. Cervical cone biopsy excises the collagen-rich component, shortens CL and is associated with earlier dilation and prostaglandin release, which are etiological moments in CI. A shorter CL <15-25 mm detected in singleton and twin pregnancies in asymptomatic or at risk pregnant women is associated with high risk and is a significant biological marker for PTD, whereas V-shaped cervical funneling has a threefold higher risk, as compared to abnormal CL. Anterior and posterior uterocervical angle, cervical volume, cervical consistency indices, identification of new maternal

and fetal genes for spontaneous PTD (SPTD) and PPROM, high fibronectin levels, vaginal pathogens, placental biomarkers in the maternal blood have a predictive role in PTD [3, 6, 7, 10, 12, 13, 14].

Preterm delivery is delivery between 22-23 + 5 g.w., the variable abortion limit, and <37 g.w. Regular uterine contractions ≥4 for 20 min with cervical changes lead to SPTD, and 75% of all PTD start either with contractions or PPROM. A significant stratification is late PTD (34-36.6 g.w.), moderate (32-33.6 g.w.), and extreme one <28 g.w. PTD rate is assessed as 5 to 10-18% worldwide and 5-10% in Europe, which is about 15 million PTDs and 1 million neonatal deaths per year. PTD is 17% for a twin pregnancy, where PTD, perinatal morbidity and mortality are considerably more frequent as compared to singleton pregnancies. It is assumed that reaching 23-26 g.w. increases the survival of premature newborns by 3%. A shorter CL in 18-24 g.w. poses 31.2–41.3% risk for PTD, and women with a previous SPTD <34 g.w. have an average risk of 20 % for SPTD <37 g.w. and 15% <34 g.w. A 4-fold increase in PTD rate <33 g.w. has been reported after cerclage, and only 1.7-fold increase after AP insertion [1, 4, 5, 6, 7, 8, 10, 12, 15, 16, 17, 18, 19].

SPTD is of heterogeneous etiology and risk factors associated with various maternal conditions – multiple pregnancy, assisted reproduction, concomitant diabetes, preeclampsia, CI; age <18 and >40, smoking, high body mass index; asymptomatic, symptomatic or vaginal or urinary infection ascending to intrauterine infection; placental abruption, enlargement of uterine myoma, multiple spontaneous abortions. Fetal growth restriction, placental, genetic, hormonal, social and ecological factors take part in the etiopathogenesis; however, idiopathic causes seem to dominate (50%) since immediate etiology cannot be defined, 25% PTDs result from emergency conditions, and PPROM constitute 25%. Uterine factors, decidual membrane activation and preterm cervical ripening, are part of SPTD pathophysiology. Cervical ripening and dilation results from decreased collagen synthesis and increased collagenase activity, vascular endothelial growth factor inducing angiogenesis and increased blood supply, increased synthesis of interleukin-6 and-8 (IL), prostaglandin and monocytic chemotaxis protein. The increased fetal risk for early and long-term complications is associated with PTD, and maternal complications involve higher rates of obstetric haemorrhages, infections, operative delivery, chorioamnionitis, endometritis, trauma, future PTD [1, 3, 4, 7, 10, 12, 15, 17, 18, 19, 20, 21, 22].

Cerclage, AP and progesterone are utilized as preventive treatment approaches in PTD to achieve suspension of a gravid cervix in high-risk and symptomatic or asymptomatic pregnant women with a short cervix. Cerclage is an effective invasive surgical procedure providing occlusion and stabilization of the incompetent cervix by means of a cervical stitch. AP is a mini-invasive alternative to cerclage, which is applicable in CI; however, the complications typical of cerclage are not frequent. t prolongs pregnancy, reduces PTD risk in singleton pregnancy; there is some controversy, although clinical effectiveness has been reported in twin pregnancy. Progesterone (as vaginal capsules or gel, as well as in dosage forms for oral, intramuscular or subcutaneous administration) provides drug-induced suspension. Antimicrobial agents, such as ceftriaxone, clarithromycin and metronidazole, have also been reported as effective against infection in 75% of cases and preventing up to 40% PTD <34 g.w.; bedrest and expectant management have also been mentioned in this respect [1, 2, 3, 4, 5, 6, 7, 8, 10, 12, 13, 16, 17, 19, 21, 22, 23, 24, 25].

REVIEW

Cerclage can achieve a 4-9 weeks latent period until delivery. In cases of previous pregnancy losses in midtrimester with painless cervical dilation, cerclage is inserted in 12-15 g.w., whereas ultrasound-indicated cerclage in CL<20 mm without cervical dilation, as well as physical examination-indicated cerclage with cervical dilation, are inserted in 16-23 g.w. Cerclage is not recommended routinely following cone biopsy because of ultrasound-demonstrated cervical vascularity and an increased risk of bleeding in uterine contractions and infection or cervical dilation larger than 4 cm. cerclage should be inserted up to 24 g.w. according to some reports, and up to 27+6 g.w., according to others. Cerclage reduces PTD rate <35 g.w. by 30%, is effective in CL <15 mm in CI and a previous PTD and has better neonatal results than progesterone in CL <8-10 mm; however, it is associated with complications – bleeding, discharge, uterine, intra-amniotic or cervical infection or rupture, PPROM, PTD, higher rates of perinatal morbidity and mortality. Evidence shows that prophylactic or rescue cerclage does not reduce the SPTD rate. The increased CL following cerclage prolongs pregnancy and the cerclage height of 18 mm cerclage – external os that is achieved reduces PTD, as compared to cerclage inserted nearer to the external os. McDonald cerclage has been reported as unable to achieve this height, and the cerclage height in the Shirodkar approach is proximally closer to the internal os, which results in CL about 5.25 mm larger than that in McDonald, with no difference in the rate of cervical rupture. The evidence regarding cerclage effectiveness in PTD <28 g.w. is insufficient. An emergency cerclage prevents amnion exposure to vaginal pathogens, which leads to the risk of PTD, PPROM or intrauterine infection, whereas history- or ultrasound-indicated cerclage provides cervical stabilization and a biochemical barrier. The benefits of total cervix occlusion remain unclear. The intersegmental angle that sums up the anterior and posterior uterocervical angle, when larger than 180°, is associated with a greater SPTD risk. Cervical models demonstrate an optimal cervix alignment to the uterine os of up to 180° and a decrease in the intersegmental angle and cervical tissue stretching is achieved 4-6 weeks following AP insertion [3, 6, 7, 8, 13, 15, 17, 18, 22, 24].

Electively, AP can be inserted in 14-16 g.w., even without anaesthesia and hospitalization under conditions of absent uterine activity and restricted physical activities, and is removed around 37 g.w. Longer exposure to AP increases the likelihood of cervical thickening and edema. The most common side effect is vaginal discharge, bleeding, or pelvic pain are less frequent, and the likelihood of cervical rupture is <0,1%. Intercourse is not contraindicated. CL is fundamental for AP insertion; AP stabilization of a previously detected funneling is verified by TVU. Ultrasound elastography seems to be able to assess the possible superiority of AP over cerclage in stabilizing collagen tissue and its compressive-preventive effect for SPTD. AP contraindications include fetal anomalies, chorioamnionitis, protrusion of membranes out of the cervix or PPROM, uterine activity predisposing to lesions and venous congestion. There are difficulties in the uterus bicollis. Pregnant women with severe uterine prolapse are at risk for uterine prolapse through the ÀÐ opening. Indomethacin and vaginal progesterone can be supplemented 24-48 hours prior to AP insertion in cases of extreme funneling and lack of internal CL but with enough external cervical tissue for the purposes of reducing the volume of amniotic liquid, decreasing the pressure on the internal os and prostaglandin release before AP insertion. The above-mentioned interval enables the application of corticosteroid prophylaxis until delivery commencement or in rapidly progressing chorioamnionitis. According to the clinical assessment, antibiotics can be added prior to, at the time of and following AP insertion. In singleton pregnancy and shortened cervix AP may be the approach of choice; in progressive shortening, supplementation of vaginal progesterone should be considered. The alternative approach is vaginal progesterone with subsequent AP or their simultaneous combination in CL <15-20 mm. The following AP mechanisms are supposed to prevent SPTD: pericervical stabilization with correction of the uterocervical angle to a narrower one; increased consistency; gravid cervix elongation. AP achieves posterior deviation of the cervical canal to the uterine os; prevents the progressive internal os dilation, which is associated with dissociation of amnion and chorion, as well as protrusion of membranes; prevents vaginal contact with intact membranes, shortening and effacement; reduces funneling. AP produces an effect on the cervical mucus plug, which is protective for intrauterine infection and is important for maintaining pregnancy and the immunological barrier. AP is likely to reduce the Ferguson reflex, resulting in oxytocin release and contractile activity [1, 3, 7, 12, 13, 16, 17, 18, 22, 23, 25].

Progesterone maintains pregnancy - it stabilizes the cervical connective tissue and reduces uterine contractions, suppresses maternal immune response against the embryo and has an immunomodulating effect. Progesterone activates the progesterone receptor, inhibits cervical ripening and dilation, whereas the drop in its levels results in cervical ripening and delivery. Progesterone reduces the expression of several proinflammatory mediators in the maternal-fetal interface (CASP11, CCL-22, ICAM1, CTLA4, NOD1 and CCL5), the myometrium (IL-33) and the cervical tissues (IL-33, IL-6, IL-12b, IL-1a, PYCARD, IL-4). The larger number of reports on progesterone recommend its vaginal administration rather than parenteral administration in history for PTD and CL £25 mm; when preventively applied in history for PTD, it reduces PTD risk < 33, 34 g.w., prolongs the gestational age, although there is controversy over its effectiveness in cases of a previous PTD. No visible effects deleterious to fetal neurodevelopment and maternal health have been reported in progesterone treatment. Preventive treatment starts in 12-14 g.w. or in cervical shortening and is applied until 34-36-37 g.w. Progesterone has been reported to be effective in PTD prevention in twins < 28-34 g.w. Progesterone seems to be ineffective in PTD prevention in twin pregnancy, in singleton and twin pregnancy, the synergic effect of AP and vaginal progesterone has been reported to prevent PTD. In a reported case of a singleton pregnancy, administration of vaginal progesterone alone proved to be insufficient in progressive cervical shortening following cone biopsy, which resulted an additional 5-10-fold increase in PTD risk. AP insertion achieved 105 days optimal latent period until delivery and prolongation of pregnancy up to 34 + 3 g.w., as well as 16 mm CL. The 16-mm cervical elongation achieved by AP following cone biopsy seems to be as effective as the verified PTD-preventive 18 mm elongation after cerclage .[6, 7, 8, 13, 16, 18, 19, 21].

AP vs standard care vs conservative or expectant management vs no treatment vs elective AP insertion

AP insertion before 14 g.w. in singleton pregnancy at high risk was reported as beneficial, with a PTD rate <34 g.w. 25.9%, ànd < 37 g.w. 50%. Another study involving a singleton pregnancy stated that compared to no treatment or vaginal progesterone alone, AP can reduce PTD risk <34, 37 g.w., but did not provide enough evidence of the AP effect on PTD, as compared to cerclage. A study of singleton and multiple pregnancies concluded that AP can prolong pregnancy, and the use of tocolytics and corticosteroids was reduced by 21% and 18%, respectively, as compared to expectant management. Another study on AP in singleton pregnancy reported reduced SPTD risk <37 g.w.Another meta-analysis supposed that AP insertion is likely to mildly reduce SPTD rate < 34 g.w. and increase the gestational age in multiple, but not in singleton pregnancy. AP insertion in singleton and twin pregnancy at risk for SPTD has a preventive effect and is a beneficial treatment regimen, as compared to no treatment at all [5, 12, 26, 27, 28, 29].

One study reported that AP did not reduce PTD by 40% or more in twin pregnancy, although a lower AP effectiveness was not excluded; PTD <34 g.w. in the AP group was 18.4%, àgainst 20.6% in the standard care group. Another report did not demonstrate PTD reduction in monochorionic diamniotic twin pregnancies requiring fetal treatment for twin-twin transfusion syndrome; PTD

< 32 g.w. was 40.3% in the AP group against 35.7% in the conservative treatment group. One study concluded that AP effectiveness is not reliable for PTD risk reduction in singleton and multiple pregnancies but reported effectiveness for risk reduction in SPTD <28 g.w. in twin pregnancies. Another report does not support AP insertion in singleton and twin pregnancies because no significant differences have been observed in PTD prevention <37, 32, 28 g.w. A study involving singleton pregnancy did not report a reduced PTD rate in prophylactic AP insertion, but in asymptomatic pregnant women with short cervix, PTD was 9.4% with AP and 5.5% without AP [19, 30, 31, 32, 33].

Progesterone vs AP

Similar PTD rates were reported in twin pregnancy - PTD <34 g.w. was 16% with AP and 22% with vaginal progesterone in CL < 38 mm; considerable benefit from AP was observed in CL < 28 mm, with PTD <34 g.w. dropping from 46% to 21%. Another report demonstrated greater AP benefits for neonatal survival and morbidity in twin pregnancy and short cervix. A report found AP no superior to vaginal progesterone in singleton pregnancy. Even in CL< 25 mm, AP seems to be less effective – 16% PTD against 4% with vaginal progesterone administration [34, 35, 36].

AP with vaginal progesterone vs vaginal progesterone vs tocolysis vs cerclage with vaginal progesterone

A study involving singleton pregnancies concluded that AP combined with vaginal progesterone achieved 7.4 % PTD <34 g.w. and was more effective than administration of vaginal progesterone alone - 17.6% PTD. Another report also found the combined use of AP and vaginal progesterone effective in preventing PTD <34 g.w. in singleton and multiple pregnancies, as compared to administration of vaginal progesterone alone. The study on AP combined with progesterone in placenta praevia reported a reduced PTD<34 g.w. and bleeding during pregnancy, as compared to using progesterone alone. Another study found a considerable difference in PTD percentage <34 g.w. in singleton pregnancies – 27.3% in progesterone, 20% in AP and progesterone before the learning curve and 4.6% after the learning curve. A study on twin pregnancies reported a similar rate, but PTD was 36.8% in AP with vaginal progesterone against 37.2% in using vaginal progesterone alone. One study did not find an advantage or considerable preventive effect in singleton pregnancies and did not report a reduction in PTD <34 g.w. in AP with vaginal progesterone, as compared to vaginal progesterone alone. A study on singleton pregnancies with short cervix comparing AP with vaginal progesterone versus tocolysis found that AP with vaginal progesterone has advantages in reducing PTD < 36 g.w. and reported 7.0% PTD, against 30.8% PTD in long-term tocolysis.

Two studies compared AP with vaginal progesterone versus cerclage combined with vaginal progesterone. One of the studies in singleton pregnancies did not find a significant difference in the gestational and neonatal results – PTD was 25% and 17% for AP with vaginal progesterone and cerclage with vaginal progesterone, respectively. A study on AP with vaginal progesterone versus cerclage with vaginal progesterone reported a 70.4% term delivery rate. In AP, there is a 1.7-fold reduction in PTD rate, and cerclage is the most appropriate approach in patients with a history of obstetric complications, CL <15 mm and large isthmic uterine fibroids.[4, 16, 18, 20, 37, 38, 39, 40, 41].

Administration of progesterone alone

One study on the administration of progesterone alone in singleton pregnancies found that following TVU measurement of CL in 20-24 g.w., SPTD <32, 34, 37 g.w. was reduced by 1.32%, and SPTD rate <34 g.w. in CL ≤15 mm with progesterone treatment was 20.4%. Another study on singleton pregnancies involving a weekly intramuscular administration of 250 mg 17-OHPC did not observe a reduction in recurrent PTD. No significant differences in PTD rate < 35 g.w. were observed in using 17-OHPC (11.0%), as compared to placebo (11,5%) [42, 43].

Cerclage vs AP

A study found that AP insertion for CI and PTD prevention <34 g.w. in singleton pregnancy was more effective than cerclage; however, in CL between 25-15 mm and <15 mm, no significant difference was observed. Another study concluded that AP is more effective than cerclage for prolongation of pregnancy in asymptomatic women with singleton pregnancy at high risk for PTD, and funneling in mid-trimester is the most important predictive marker. A report did not find significant differences for PTD <34 g.w. in singleton pregnancies treated by AP or cerclage, although funneling combined with AP resulted in a lower PTD rate < 34 g.w. – 26.5 %, as compared to funneling with cerclage – 37.1%. Another report on singleton pregnancy also found similarity and presented AP as an alternative to McDonald's cerclage, and PTD rate <37, 34 g.w. was similar in both groups, each of which received 80 mg vaginal progesterone as a gel. A study also found them equally effective for prologation of pregnancy in CI and PTD risk - by 12.1 weeks for AP and and 13.4 weeks for cerclage. The largest randomized controlled study recorded equal effectiveness and concluded that AP is non-inferior to cerclage in women with a previous SPTD and shortened cervix. Another report involving singleton pregnancies also found that AP is as effective as cerclage [1, 10, 11, 14, 17, 44, 45].

AP with cerclage vs cerclage alone vs AP alone

A report involving singleton pregnancies compared cerclage-AP combination (27.7% PTD) and cerclage used alone (32.4% PTD) and concluded that the combined approach has benefits, especially in protruding amnion. Another study on singleton pregnancies found the cerclage-AP combination achieves a gestational age of 38.33 g.w. and is more effective than treatment with either cerclage (37.82 g.w.) or AP alone (35.73 g.w.) [46, 47].

Cerclage vs another cerclage technique vs cerclage with antibiotics and tocolysis

A study involving singleton pregnancies con-

cluded that Shirodkar cerclage reduces PTD rates <35, 34,32 g.w., as compared to McDonald cerclage. The two cerclage techniques did not demonstrate a difference in PTD < 28 g.w., and the PTD rate < 37 g.w. was not in favour of any of the surgical techniques. Another report comparing transabdominal cerclage or high vaginal cerclage to low vaginal cerclage concluded that transabdominal cerclage is superior to low vaginal cerclage, with PTD <32 g.w. 8% against 33%, respectively. No difference in PTD rate was observed between high vaginal cerclage (38%) and low vaginal cerclage (33%). Due to a lack of evidence, one of the reports could not assess whether cerclage combined with antibiotics and tocolysis has advantages over treatment with cerclage alone for preventing SPTD [15, 24, 48].

Combined approaches or studies comparing several treatment regimens

A study comparing 4 approaches in singleton pregnancies presented the following PTD rates: 44.4 % in AP with cerclage and vaginal progesterone; 32.5% in AP with vaginal progesterone; 36.8% in cerclage with vaginal progesterone; 32.7% in the administration of vaginal progesterone alone. The combined regimen could prolong pregnancy until term, but SPDT rate <37 g.w. was found to be similar in all groups. In a study on singleton pregnancies comparing 4 approaches, e.g. involving progesterone, cerclage, AP, cerclage and AP, the PTD rate found was 43.6%, 45.5%, 61.1% and 50.0%, respectively. The group treated with progesterone alone showed the lowest PTD rate, which lead to the conclusion that progesterone supplementation is fundamental for PTD prevention; however, in short, gravid cervix PTD rate remained high. Another study on singleton pregnancies, comparing vaginal progesterone, oral progesterone (17á-hydroxyprogesterone caproate), cerclage and AP came to the conclusion that vaginal progesterone administration is the only intervention of consistent effectiveness for PTD prevention <34, 37 g.w., whereas 17-OHPC reduces PTD <37 g.w. In another study, the combined treatment involving AP, progesterone, and cerclage did not show a considerable effect on reducing PTD in twins compared to placebo. A study on singleton and multiple pregnancies involving AP, progesterone alone, AP with progesterone and expectant management came to the conclusion that combining AP treatment with other ones, such as progesterone, does not provide reliable evidence in support of positive results [2, 6, 7, 49, 50].

No consensus has been reached regarding the need for CL measurement, the range 15-25 mm is considered the cutoff for cervical shortening. In singleton pregnancy without PTD history and with CL ≥25 mm, prophylactic treatment should not be applied - this is the only absolute consensus that can be found at present. In asymptomatic women with singleton pregnancy, without previous SPTD and with CL ≤25 mm <24 g.w., vaginal progesterone administration until 34-36 g.w. is most frequently recommended. The recommendations vary according to CL < 25, 20, 15 mm, but cerclage combined with progesterone is recommended in CL <10 mm. In singleton pregnancy with a history of 1 or 2 previous PTD, PPROM or late spontaneous abortions and CL <25 mm, all guidelines recommend one or another type of cerclage and progesterone treatment is an option, an alternative or combination. In cases of cervical dilation, emergency cerclage is recommended, as well as vaginal progesterone in the period 16-36 g.w., follow-up or treatment in CL ≤25 mm. For twin pregnancies with or without a history of PTD and CL ≥ or < 25 mm, the greater part of the guigelines are against prophylactic or active treatment. The other instructions recommend progesterone generally administered by the vaginal or parenteral route, with or without AP, with cerclage in the presence of risk factors, although some authors restrain from giving recommendations. In spite of the PTD risk, the dominating part of the studies do not recommend treatment - cerclage is not recommended even in the shortened cervix but in cervical dilation < 24 g.w. emergency cerclage should be considered. AP is not recommended in twin pregnancy and short cervix for PTD prevention. A systematic review has demonstrated that vaginal progesterone administration in midtrimester in asymptomatic women with twin pregnancy and short cervix significantly reduces PTD risk in the period 28 - 34 g.w. There is consensus on abdominal cerclage as a treatment option following unsuccessful vaginal cerclage or cervical amputation. Combining 2-3 treatment options is not recommended.

There is insufficient evidence on using AP as a standard treatment in singleton and twin pregnancy, irrespective of cervical length and PTD history, with regard to PTD prevention and improvement of neonatal results. The evidence does not refute utilizing AP, but only a few reports compare AP with other treatment options or make definitive conclusions on the significant superiority in the effectiveness of any other approach over AP for the prevention of PTD and late abortions. According to one report, AP has been certified for SPTD prevention, and grounds have been presented for its use and implementation in clinical practice; 89% of pessary-treated women would recommend it because it is well-tolerated and easily used [6, 7, 8, 10, 17, 22, 25, 51].

RESULTS

The present review covers the study of AP used in different treatment regimens and compared to different approaches, with the dominant part of the research reporting AP benefits for gravid cervix suspension based on PTD results before 34 g.w. under under conditions of shortened cervical length in singleton and twin pregnancies.

In singleton pregnancies, the lowest PTD rate for AP combined with cerclage and vaginal progesterone is 44.4%, PTD <37 g.w.; for long-term tocolysis - 30.8%, PTD <36 g.w.; for transabdominal cerclage - 8%, PTD <32 g.w. For cerclage alone, the lowest PTD rate <34 g.w. is 32.4%, for cerclage combined with AP - 27.7%, and for cerclage/vaginal progesterone combination - 17%. For indicated AP, the percentage is 16%, and for electively inserted one, it is 9.4%. For AP combined with vaginal progesterone,

the value is 4.6%, and for vaginal progesterone alone it is 4%. In this review, the lowest PTD rate <34 g.w. reported for AP used alone in multiple pregnancies is 18.4%. [2, 4, 19, 33, 36, 39, 41, 46, 48]

CONCLUSION

No approach is excluded in the management of isthmico-cervical incompetence in the attempt to regulate preterm delivery rates; however, 89% of women treated by ARABIN pessary recommend it. The evidence does not refute its use, but the number of reports comparing it with other treatment options is scarce. Treatment with vaginal progesterone alone proves to be insufficient in progressive cervical shortening; the 16 mm cervical elongation achieved by AP following cone biopsy seems to be as effective as the verified PTD-preventive one following 18 mm cerclage and suffices for optimal cervical stabilization and latent period until delivery.

ARABIN pessary is superior or non-inferior to cerclage in incompetent cervix in singleton pregnancies because of the similarity in PTD results; however, there is evidence that its effectiveness prevails over vaginal progesterone in twin pregnancies where a non-active approach is preferred. ARABIN cerclage pessary combined with vaginal progesterone destabilizes the non-significantly prevailing effectiveness of vaginal progesterone administered alone in singleton pregnancy. AP is not included in the guidelines as a standard treatment, although research findings suggest it is likely to be implemented as a principal recommendation in the future for gravid cervix suspension, either in combination or alone.

Abbreviations:
AP - ARABIN pessary,
CI - cervical incompetence,
CL - cervical length,
g.w. - gestational week,
17-OHPC - 17α-hydroxyprogesterone caproate,
PTD - preterm delivery,
PPROM - preterm premature rupture of the membranes,
SPTD - spontaneous PTD,
TVU - transvaginal ultrasound,

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Please cite this article as: Telbiyska K, Angelova M. Stratification of Gravid Cervix Suspension – a Review. *J of IMAB*. 2025 Jan-Mar;31(1):6029-6036. [Crossref - https://doi.org/10.5272/jimab.2025311.6029]

Received: 15/08/2024; Published online: 27/02/2025

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