Preterm Prevention Clinic Treatment Pathway

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Approved by Maternity Governance Meeting on:	19th June 2020
Review Date This is the most current document and should be used until a revised version is in place:	15th November 2022

Key Amendment

Date	Amendment	Approved by
19th June 2020	New document approved	Maternity Governance meeting

Background:

Every year worldwide approximately 13 million premature deliveries babies are born premature, with a global incidence of up to 12%. Preterm birth is defined as birth before 37 weeks' gestation. It is a major contributor to neonatal and infant morbidity and mortality[1]. Spontaneous preterm birth accounts for about three-quarters of these births and births before 30 weeks of gestation account for most neonatal deaths[2]. The costs of preterm labour are significant, costing the US economy 26.2 billion dollars in 2005. The rate of spontaneous preterm birth in 2017 at Worcestershire Acute Hospitals Trust was around 9%. Preterm birth also has marked psychological, physical and emotional sequelae for those families affected[3].

The incidence of spontaneous preterm birth is continuing to rise. The reasons driving this increase remain unclear[4]. There are certain clinical measures employed that aim to prevent preterm labour, although most of these are still under evaluation. Nevertheless, current interventions could potentially eliminate up to 50% of recurrent preterm births[4]. Management needs to target those women at greatest risk of preterm delivery in order to improve care and ultimately outcome for both mother and baby. Interventions such as cervical cerclage, pre-delivery steroids for fetal lung maturation, progesterone, antibiotics, tocolytics and timely in-utero transfer may form part of a broader package of care offered to women demonstrated to be at greatest risk of early delivery.

Women with a history of a previous preterm labour or a second trimester loss are at high risk of having a further preterm delivery[5]. Other risk factors include previous cervical surgery, terminations of pregnancy, repeated dilatation and curettage and trachelectomy[6].

There are many other "softer" risk factors implicated in the pathogenesis of preterm labour. These include age, parity, body mass index, ethnicity, socio-economic status, smoking, anxiety and depression also associated with premature labour[5]. The most challenging element of this clinical conundrum is that preterm delivery is a multifactorial problem, with multiple aetiologies.

More recently, the "Saving Babies Lives Bundle version 2" has reiterated the importance of reducing preterm birth and through its 5th element made it a requirement to formalise the risk assessment and management of women at risk. As part of this, the prediction of women at

greatest risk is of paramount importance. Interventions to reduce risk can then be implemented.

Prediction of Preterm delivery:

Cervical sonography:

The cervix provides mechanical strength and helps to prevent ascending infection from the vagina penetrating the intra-uterine space. Cervical insufficiency, categorized as painless cervical dilatation, is the inability of the uterine cervix to retain a pregnancy in the absence of contractions or labour. Transvaginal ultrasound is the gold standard for assessment of cervical length. It has been reliably shown that the shorter the sonographic cervical length in the mid-trimester, the higher the risk of spontaneous preterm labour, presumably due to an "insufficient cervix"

There is no consensus as to what constitutes a sonographically short cervix. Some studies use a cervical length of <25mm, whilst others reduce this further to <15mm. Despite this clinical conflict, a shortening cervix remains the single most powerful predictor for preterm birth in the index pregnancy. Furthermore, a shortening cervix is far more informative than a history of previous preterm birth. With shortening of the cervix to <15 mm, there is almost a 50% risk of preterm birth at 32 weeks[7]. Therefore, through cervical length screening, interventions should be offered to those women at greatest risk in a timely fashion[8].
Nevertheless, the use of cervical length scanning as a risk assessment tool has its limitations when used in isolation. Previous studies by Romero et al. indicate that only 8% of all patients with a mid-trimester cervical length ≤15mm 9 deliver preterm at <32 weeks' gestation.

Interventions for the prevention of preterm birth:

Interventions available at Worcester Royal Hospital for the prevention of preterm birth include:

- Cervical Cerclage
- Progesterone
- Aspirin

Cervical cerclage

Cervical cerclage involves the insertion of a surgical suture in the hope of being able to reinforce the mechanical strength of a shortening cervix. This can either be done as an emergency rescue procedure or as a planned prophylactic intervention for a woman with a poor previous obstetric history.

Emergency cerclage:

These should only be inserted where a patient presents at <24/40 gestation with a dilated cervix with intact membranes, in the absence of bleeding or contractions. It is crucial to assess for maternal well-being through basic observations and measurement of the CRP and white cell count. Where there is concern over possible sepsis, cerclage should be omitted. Patients should be thoroughly counseled regarding the risks of cerclage (bleeding, rupture of the membranes and subsequent infection) together with the potential that it may not ultimately.

Patients should remain as inpatients following the procedure for at least 3 days to watch for the development of sepsis. Four hourly observations and daily white cell counts should be taken following cerclage for three days. Should a patient experience ruptured membranes with a cerclage in situ, the stitch should be removed to minimize the risk of ascending infection on the clear counselling that this may result in preterm labour or late trimester miscarriage.

Evidence:

The Vaginal Ultrasound Cerclage Trial compared women who had received cervical cerclage with those who had not. Recurrent preterm birth (≤35 week's gestation) occurred in 32% of women with a cervical cerclage, compared with 42% of those who did not receive cerclage (OR, 0.67; 95% CI, 0.42–1.07; P 053)[14]. The incidence of preterm birth (≤35 weeks gestation) was particularly decreased in the 64 women whose cervical length was less than 15mm at randomization, who subsequently received cerclage. Women with cervical lengths between 15 and 25mm treated with cerclage delivered infants with significantly less morbidity[14]. Historically other studies have found no benefit from cervical cerclage, but this may relate to the previous inability to predict preterm labour and therefore patient mix within

the trials. Consequently, cerclage does remain a controversial intervention, although the Royal College of Obstetricians and Gynecologists recommend its use in women with a history of preterm labour and a cervical length of <25mm[8].

Results from randomized trials show similar rates of preterm birth in women with prior preterm births who undergo a history-indicated, prophylactic cerclage compared with those followed by ultrasound who were treated with cerclage only if the cervix shortened.

Therefore, cervical surveillance using transvaginal scanning can help to select appropriate candidates who would benefit most from cerclage, thus reducing needless surgical intervention and its complications.

Complications of cerclage are not inconsiderable and include infection, risk of bleeding, risk from the anaesthetic and also potential increased risk of miscarriage. As such, it is an intervention that should only ever be targeted at those for whom the risk of preterm delivery is significant and in whom the potential for benefit is greatest.

Progesterone:

Two progesterone dosage forms are used to reduce preterm labor; a natural progesterone administered vaginally, and 17-alpha hydroxyprogesterone caproate (17P), a synthetic progestin, administered via the intramuscular (IM) route.

There is now sufficient evidence from at least 6 trials to support the prophylactic use of 17 alpha-hydroxyprogesterone caproate (17P), 250 mg given intramuscularly, weekly between 16 and 36 weeks, to women with prior spontaneous preterm birth between 20 and 36 weeks. This therapy reduces the risk of recurrent preterm birth by approximately 35% and is especially effective for women with a prior early preterm birth [15-19].

There is also evidence that vaginal progesterone reduces the risk of recurrent preterm birth[20-22]. In a trial sponsored by The Fetal Medicine Foundation, the overall reduction of preterm birth with vaginal progesterone administered in women with a cervical length of <15mm was 44%[21]. These results have been replicated by others studies[22-23].

NICE recommend the use of vaginal progesterone in certain situations (see below). This decision should be made following counselling of the woman by a Consultant.

- Offer a choice of prophylactic vaginal progesterone or prophylactic cervical cerclage to women who have both:
    - a history of spontaneous preterm birth (up to 34+0 weeks of pregnancy) or mid-trimester loss (from 16+0 weeks of pregnancy onwards) and
    - results from a transvaginal ultrasound scan…. that show a cervical length of 25 mm or less. Discuss the risks and benefits of both options with the woman, and make a shared decision on which treatment is most suitable. [2019]
- Consider prophylactic vaginal progesterone for women who have either:
    - a history of spontaneous preterm birth (up to 34+0 weeks of pregnancy) or mid-trimester loss (from 16+0 weeks of pregnancy onwards) or results from a transvaginal ultrasound scan carried out between 16+0 and 24+0 weeks of pregnancy that show a cervical length of 25 mm or less. [2019]

Aspirin:

Aspirin is recognised to reduce the risk of pre-eclampsia (16 fewer per 1000 women treated), preterm birth (16 fewer per 1000 treated), the baby being born small-for-gestational age (seven fewer per 1000 treated) and fetal or neonatal death (five fewer per 1000 treated). Overall, administering antiplatelet agents to 1000 women led to 20 fewer pregnancies with serious adverse outcomes.

Aspirin slightly increased the risk of postpartum haemorrhage (>500 mls). Antiplatelet agents marginally increase the risk of placental abruption, but again the quality of the evidence was moderate due to low event numbers and thus wide 95% CI. Overall, aspirin is considered to improve outcome and appears to be safe.

Preterm Prevention Clinic (PPC)

The Preterm Prevention Clinic at Worcester Royal Hospital will see women as soon as possible following booking at around 14 weeks gestation. These women will have been referred from the community if risk factors for preterm delivery have been highlighted (see below).

During this appointment, women would be assessed for clinical risk factors for preterm birth. Depending on the history women may be offered a prophylactic cerclage +/- progesterone supplementation. Women who have had a failed cerclage in the past should be discussed with Birmingham Women's Hospital.

Irrespective of the presence of a suture, transvaginal ultrasound assessment of the cervix will be performed at the 18 week review. If the cervix is found to be short, i.e. measuring <25mm, the patient will be offered FFN swab testing. Using the QUiPP algorithm, the FFN result will be combined with the cervical length to generate a risk of delivery. Following discussion, the patient may be offered further surgical or medical intervention in the form of cervical cerclage or vaginal progesterone treatment. Women would be seen again at 22 weeks and again at 24 weeks.

Women who have undergone screening and have had no intervention may be transferred back into routine care from 24 weeks gestation. Midwifery care is appropriate should there be no further risk factors.

Women who have undergone an intervention e.g. cerclage or progesterone therapy should remain under the Preterm Prevention Clinic until 36 weeks.

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Flow chart for Preterm Prevention Clinic

Offer prophylactic Cerclage/Arabin following first trimester screening if history of preterm delivery or mid-trimester loss with evidence of cervical incompetence as soon as possible

General principles

BP

Urine dip/Send MSU

TV USS from 18 weeks

Fetal Fibronectin (FFN) if cervical length <25mm on TV USS

Generate QUiPP risk

If shortening cervix (<25mm) discuss Options if +ve FFN:

- Cerclage
- Arabin
- Progesterone

Not for cerclage after 24/40

Arabin pessary ok >24/40

From >23/40 consider Steroids and Magnesium if delivery thought imminent (refer to QUiPP result_

Dalacin cream 0.5mg PV nocte for 7 days at 18/40 and 22/40.