

Progesterone treatment for women suffering bleeding in early pregnancy

The National Institute for Health and Care Excellence, (NICE) has updated its guidance for the treatment of miscarriage and threatened miscarriage. It now recommends offering women who have bleeding in early pregnancy and who have suffered at least 1 miscarriage in the past, Progesterone in the form of vaginal tablets taken twice a day up to 16 weeks in order to improve the likelihood of delivering a live baby past 24 weeks. The early pregnancy assessment unit at the Royal Devon and Exeter hospital, is following this guidance and will prescribe Cyclogest, a natural Progesterone in the form of a vaginal tablet of 400 mg, to be placed within the vagina morning and evening each day up to 16 weeks. This for women who present to our unit with bleeding in early pregnancy, and a scan showing a pregnancy sac within the womb, (whether a heartbeat is seen or not) where there has been at least 1 miscarriage in the past. The guidance does not recommend Progesterone for women who have bleeding in early pregnancy, but have never miscarried in the past, or women who are not bleeding but have had a history of recurrent miscarriages, as there is no proven benefit.

The absence of benefit for such women appears confusing, hence we have prepared this information leaflet to better inform those who are anxious about their risk of miscarrying, and whether vaginal Progesterone is safe for them, or if it might provide benefit. There has not been evidence of significant harm to women or unborn babies in early pregnancy from vaginal Progesterone, however long term data of large numbers of children whose mothers received progesterone in the early stages of pregnancy when all the body parts were developing, is not available.

Although the guidance suggests there is benefit for all women with bleeding who have previously miscarried, the overall benefit is mainly seen in women who have had 3 or more previous miscarriages.

The NICE Guidance is mainly based on a review of all recent high-quality trials examining the use of Progesterone for women with problems of early pregnancy. This is called a Cochrane systematic review and brings together all the results to form a single but more powerful conclusion. The full guidance is available here.

www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013792.pub2/epdf/full

The individual trial with the greatest influence on the nice guidance was The PRISM study 2019

www.nejm.org/doi/pdf/10.1056/NEJMoa1813730

A simplified summary of the data is enclosed below.

Overall this study did not result in improvement in live births with Progesterone for all women with bleeding in early pregnancy. It was however a study of sufficiently large size that smaller individual groups of women could be analysed, principally groups of women who had previously had different numbers of miscarriages.

For women with bleeding in early pregnancy who had never miscarried before, there were slightly more miscarriages in the group given Progesterone, however the number was so small that it could not provide evidence to influence decision making. In statistical terms this is said to

be non -significant.

For women with bleeding in early pregnancy, who had had 1 or 2 previous miscarriages, there was an observed improvement in live birth rate, equivalent to approximately 3-4 more live births per 100 women, which almost reached significance in statistical terms. This means the benefit has not been definitely proven by this study.

For women with bleeding in early pregnancy who had had 3 or more previous miscarriages, there was a significant improvement in live birth rate when given vaginal Progesterone, equivalent to approximately 14-15 more live births per 100 women.

Number of previous miscarriages	Live births / total (no progesterone)	Live births / total (+ progesterone)	Risk ratio	Estimated change in live births expected for a group of 100 women
0	840 / 1127	824 / 1111	.99	No change (0.37 less)
1-2	534 / 738	591 / 777	1.05	3.7 more live births
3 or more	84 / 148	98 / 137	1.28	14.7 more live births

I hope you find this information helpful in understanding her why Progesterone may or may not of benefit to you if you are suffering bleeding in early pregnancy. If you have anything more you wish to discuss, please don't hesitate to ask our specialist nurses / doctors.

Whether or not you choose to take Progesterone in early pregnancy this will not affect the ongoing and supportive care provided by the early pregnancy assessment unit.

The Trust cannot accept any responsibility for the accuracy of the information given if the leaflet is not used by Royal Devon staff undertaking procedures at the Royal Devon hospitals.

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