EPiC2 PPI summary

What is the research about?

Endometriosis affects 10% of women and those assigned female at birth. Endometriosis is where cells similar to those lining the womb (the 'endometrium') grow elsewhere in the body, forming so called endometriosis 'lesions'. Most commonly the lesions grow on the lining of the pelvic cavity (the space around the womb, bowels and bladder) and this is called 'peritoneal' endometriosis. Endometriosis can cause terrible pelvic pain, pain with periods, pain with sex, pain opening the bowels and passing urine, and difficulty getting pregnant. There is no cure for endometriosis, and we do not know what causes it, or why some women get it. Current treatments for endometriosis include surgery to remove the lesions and hormone treatments that stop the ovaries producing estrogen. Surgery for endometriosis carries risks, does not always work, and sometimes needs to be repeated. Only one third of women feel that hormone treatments are helpful and many experience unpleasant side effects. Women with endometriosis want better medical treatments and pain management.

Work in our laboratory at the EXPPECT Centre at the University of Edinburgh, funded by previous grants from Wellbeing of Women, has shown that cells from the pelvic wall of women with peritoneal endometriosis have a different metabolism compared to women without disease. The cells produce higher amounts of lactate - similar to the behaviour of cancer cells. When we treated pelvic cells from women with peritoneal endometriosis with a drug called dichloroacetate, they were found to return to normal metabolic behaviour. We also noted that dichloroacetate had an impact on lactate production and on the growth of endometrial cells grown together with pelvic cells from women with disease. Further testing in mice with endometriosis found that dichloroacetate, after seven days of treatment, caused a marked reduction in pelvic lactate concentrations and the size of the lesions. Dichloroacetate is a drug that is used to treat rare metabolic disorders in children and has previously been investigated as a cancer treatment.

Following these laboratory studies, we treated 30 women with endometriosis with dichloroacetate (a trial called EPiC1). The women in this small trial reported that they had less painful symptoms and required fewer painkillers when they were taking dichloroacetate. Some of the women described the treatment as "life changing" but some women had mild side-effects, like heartburn/nausea or tingling in their fingers.

We now plan to test dichloroacetate in a bigger trial (called EPiC2) of 100 women from two Scottish hospitals with endometriosis and compare it to a placebo ('dummy' tablets).

Aims of the study

The aim of the EPiC2 trial is to find out what dose of dichloroacetate has the most impact on painful endometriosis symptoms and has the fewest side-effects. The data from EPiC2 will also help plan a future larger UK-wide trial to truly determine whether dichloroacetate can reduce endometriosis-associated pain, improve quality of life and provide value for money.

How will we go about the research?

Women with endometriosis being treated at two hospitals will be provided with information about our trial. If they wish to take part, they will be asked to sign a consent form. They will then be allocated at random to take dichloroacetate or placebo tablets for 12 weeks. This is the fairest way of testing a new treatment. Neither the doctor nor the participant will know whether they are taking dichloroacetate or placebo. Before starting treatment, they will be asked for a blood sample so we can perform a genetic test, to see whether dichloroacetate leaves the body quickly or slowly. This will help us to decide which dose of dichloroacetate they should receive. After six weeks on the allocated drug, the women will be allowed to increase the dose of the drug, or stay on the same dose, depending on the impact it has had on their pain and what side-effects they are experiencing. We will ask all of the women in the trial to complete questionnaires about their pain and other symptoms at the beginning, middle and end of the trial. We will also take three further blood samples to check the blood levels of dichloroacetate during treatment. We have involved a group of women with lived experience of endometriosis for advice about how to design our trial and we will ask them to continue to provide advice throughout the trial. They will receive honoraria for their time. All of the information that we collect in EPiC2 will be analysed to help us find out what dose of dichloroacetate has the most impact on painful endometriosis symptoms and has the fewest side effects, and help us design the future definitive trial.

What potential impact will our research have on women and girls?

More than 190 million women suffer from endometriosis yet few people have heard of it and treatment, which can impact fertility, has progressed very little for over 40 years. We believe that dichloroacetate could help alleviate endometriosis pain in women who cannot - or do not wish to - take hormonal treatments. EPiC2 is a crucial step in moving our exciting research from the laboratory into clinical practice. Once we have shown, in EPiC2, what dose of dichloroacetate has the most impact on painful endometriosis symptoms and has the fewest side-effects, we will apply for further funding to carry out the larger clinical trial across the UK to truly determine whether dichloroacetate can reduce endometriosis pain and provide value for money. Assuming that we will complete EPiC2 in 2025, our larger trial could provide definitive results by 2030. If dichloroacetate is shown to be truly effective, we will ensure that it is rapidly incorporated into national and international recommendations for the treatment of women with endometriosis.