Improving the Diagnosis and Treatment of Endometriosis

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Medical Research Future Fund

This study has been approved by the Austin Health Human Research Ethics Committee
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Partnering Institutions:

Background

More than 10% of Australian women suffer from endometriosis and pelvic pain at some point in their lives. Symptoms are variable, but can result in debilitating pain and troubles with fertility, along with negative effects on mental health, relationships and financial stability.

Our research team aims to improve the quality of life for all women living with endometriosis through research-driven improvements to diagnosis and treatment. Our nine coordinated projects focus on 3 major themes:

1. Better diagnosis of initial and recurrent endometriosis
2. Improved outcomes for women with endometriosis-related pain
3. Development of evidence-based pathways to treat endometriosis-related infertility.

The 3 themes contain a powerful mixture of clinical trials and lab-based research that will lead to improved outcomes in conjunction with a better understanding of factors that lead to the development and progression of endometriosis.

Project 1:

Developing and evaluating a screening tool to improve pre-operative prediction of absence of endometriosis in women with pelvic pain

Pelvic pain is a very common issue for women. Endometriosis is a common cause of pelvic pain but currently, in most cases, in order to diagnose endometriosis a woman needs to have a laparoscopy (key-hole surgery). While ultrasound can usually pick up endometriosis cysts on ovaries (endometriomas) and larger areas of deep endometriosis, it cannot see superficial (surface) endometriosis which is the most common type. When laparoscopies are undertaken to look for endometriosis in women with pelvic pain, approximately one third will not have endometriosis. That means one third of women having a laparoscopy for this reason will have put themselves through surgery without the possible benefits.

We plan to make an 'endometriosis calculator' that uses questions about a woman's symptoms and medical history, to give them a better idea about their chance of having endometriosis before they have an operation. This will be used as a tool to help women decide if they want to go on and have a laparoscopy or not. Its purpose is to result in fewer women having unnecessary surgery and getting more appropriate treatment for their pain instead.

In this study we will look at women already planning to have a laparoscopy for investigation of their pelvic pain. We will ask them to fill in a questionnaire about their symptoms and medical history before their operation and then we will check if they had endometriosis at surgery or not. We will use this information to develop a questionnaire that can predict if a woman is less likely to have endometriosis.

Are you interested? Are you eligible to participate in this project?

If you are planning to have a laparoscopy (key-hole surgery) for pelvic pain to see whether or not you have endometriosis, you may be eligible.

What happens if I participate in this project?

You will be asked to answer an online questionnaire before your laparoscopy and the findings at your surgery will be recorded.

There will be no change to your treatment and there will be no extra visits required.

Project 2:
Predicting recurrence of endometriosis

Following surgery to diagnose and treat endometriosis, patients have a 6-67% chance of requiring another operation because the endometriosis returns (recurrent disease). Our previous research, conducted at The Royal Women's Hospital, has identified certain clinical features that are associated with endometriosis recurrence; these features include basic demographic information like age, ultrasound findings, pathology results and observations made by a gynaecologist during previous surgery to treat endometriosis.

The goal of our research is to develop a prediction tool or questionnaire, to be used by doctors in their consultations with patients diagnosed with endometriosis for predicting the likelihood of endometriosis returning. Such a tool will allow the treating clinical team to tailor management and treatment options and monitor disease progression in those at risk of recurrence.

In this study we will look at patients already planning to have a laparoscopy for investigation of their pelvic pain. We will collect medical information from hospital records and ask participants to complete a questionnaire about their medical history and symptoms before their surgery. We will use this information to develop a questionnaire-based prediction tool that can predict if an endometriosis patient is likely to experience recurrence of disease.

Are you interested? Are you eligible to participate in this project?

If you are planning to have a laparoscopy (key-hole surgery) for pelvic pain, you may be eligible.

What happens if I participate in this project?

You will be asked to answer an online questionnaire before your laparoscopy and the findings at your surgery will be recorded.

There will be no change to your treatment and there will be no extra visits required.

Project 3:

The role of epithelial somatic mutations in endometriosis recurrence

Recently, areas of endometriosis were shown to have somatic mutations (these are small changes in the the building blocks of body cells that increase the cell's survival, growth and 'stickiness') which contribute to the formation of endometriosis.

However, we do not know what role these changes play in the severity of endometriosis or the risk of endometriosis returning after surgery.

In an attempt to answer these questions and develop predictive tools for endometriosis recurrence, this project will involve the use of tests on cells isolated from our archived endometriosis lesions that are housed in our Women's Biobank. This Biobank currently holds over 900 patient samples collected during laparoscopic surgery and is a valuable resource for improving our understanding of endometriosis.

Over the next five years, we will be asking participants from our projects to contribute to this Biobank through the donation of endometriosis tissue and other samples removed at time of surgery so we can continue to improve our understanding of endometriosis even more. By contributing to the Biobank, you will be ensuring the future of endometriosis research to find the answers urgently needed to stop endometriosis in its tracks.

Are you interested? Are you eligible to participate in this project?

Depending on your enrolment in other projects in this study group, you may be eligible.

What happens if I participate in this project?

During your laparoscopic surgery, extra small samples will be taken for this research.

There will be no other change to your treatment and there will be no extra visits required.

Project 4:
Endometriosis lesion biomarkers

Formal diagnosis of endometriosis requires surgery. There are no diagnostic blood tests for the condition because biomarkers of endometriosis have not been identified yet. We believe that endometriotic lesions (growths formed in the pelvic cavity in patients with endometriosis) will provide researchers the best clues about which biomarkers are present in high enough numbers to be suitable as a blood test to diagnose endometriosis. This would mean patients with endometriosis would not have to undergo invasive surgery to receive a diagnosis.

The goal of our research is to identify 'endometriosis biomarkers' (which are substances present in blood or other body tissues) that can be measured in a simple blood test that will help to diagnose endometriosis without the need for surgery. In this study we will look at patients already planning to have a laparoscopy for investigation of their pelvic pain. We will collect medical information from hospital records and ask participants to complete a questionnaire about their medical history and symptoms before their surgery. We will also ask patients to donate a small blood sample, or a tissue sample (endometriotic lesion or a sample of peritoneal tissue) or a sample of peritoneal fluid (the fluid surrounding the pelvic organs in the abdominal cavity). We will use this information and the donated biological specimens to identify biomarkers that originate from endometriotic lesions and can be used as a diagnostic blood test to identify endometriosis.

Are you interested? Are you eligible to participate in this project?

If you are planning to have a laparoscopy (keyhole surgery) for pelvic pain and would be interested in donating a small blood and or tissue sample to our research, you may be eligible.

What happens if I participate in this project?

Small amount of blood will be taken from you before your laparoscopy while you are under anaesthetics (asleep) and small tissue samples will be taken during your surgery.

There will be no other change to your treatment.

Some patients who enrol in this study may be asked to return to the hospital to donate extra blood samples following their surgery.

Project 5:

A possible novel treatment for endometriosis: palmitoylethanolamide and polydatin - a double blind randomized controlled trial

Effective medical therapies for the treatment of endometriosis-related pelvic pain are limited and are often associated with side-effects.

Palmitoylethanolamide (PEA) is a food supplement that has been shown to reduce inflammation. Polydatin (PLD) is also a food supplement that has antioxidant and pain reduction properties. There have been some small studies performed to assess if the combination of PEA/PLD is helpful for persistent pain associated with endometriosis. The results suggest it might have benefit, but further studies are required.

Multiple studies that assessed PEA/PLD for pain relief in various other pain conditions have not reported any significant side effects.

The aim of this study is to determine if treatment with PEA/PLD improves endometriosis associated pain.

Women who are booked for surgical treatment of endometriosis will be offered participation in this study. Participation will not change their surgeon's care plan. The participants will be randomised to either receive 8 weeks of PEA/PLD treatment or placebo prior to their surgery. The endometriosis will then be confirmed or excluded during the surgery.

Lesions of endometriosis, endometrium, pelvic fluid and blood will be collected where possible to assess inflammatory markers.

We will assess the change in pain scores and quality of life scores between the 2 groups to see if PEA/PLD is beneficial.

Are you interested? Are you eligible to participate in this project?

If you are planning to have a laparoscopy (key-hole surgery) for pelvic pain and are booked for it in more than 2 months' time, and you will use reliable contraception in the 2 months before surgery, you may be eligible.

What happens if I participate in this project?

You will be asked to answer an online questionnaire before starting treatment with either PEA/PLD or placebo (you will not know which one). You will take the treatment for 8 weeks and there will be another questionnaire after the treatment but before surgery. The third and last questionnaire will occur 4 months after surgery. Findings at your surgery will be recorded.

Your surgical wait time will not be altered.

Your surgical treatment will be the same as planned and based on the findings during the surgery. Tissue samples removed as part of your treatment will be taken for the study.

A single additional blood sample will be taken for the study.

There will be no extra visits required.

Project 6:

Cellular mechanisms underlying palmitoylethanolamide/ polydatin treatment

This project is paired with Project 5. Researchers will endeavour to better understand the effect of PEA/PLD on endometriosis and endometrium at a molecular or microscopic level.

During surgery, small samples of endometrium and endometriosis tissue will be collected as part of your routine surgical treatment, to investigate the effect of the PEA/PLD treatment on gene expression (the ability for the building blocks of cells to create different effects on the body). To do this Next Generation Sequencing (NGS) will be performed on the samples taken from surgery. This will be followed by several laboratory based tests on the endometriosis tissue.

The outcomes of this project aim to demonstrate the most significant mechanisms that contribute to PEA/PLD function and help us to further understand more about how and why endometriosis and pain coexist.

Are you interested? Are you eligible to participate in this project?

This project is paired with Project 5.

What happens if I participate in this project?

During your laparoscopic surgery, extra small samples will be taken for this research along with a single blood sample.

There will be no extra visits required.

Project 7:

Pelvic floor muscle tenderness and pelvic pain in women undergoing surgery for endometriosis

Women with pelvic pain, including women with pelvic pain associated with endometriosis, often have pelvic floor muscle tenderness and tension. These problems may be related to their pelvic pain continuing, despite medical or surgical treatments for endometriosis.

This project aims to identify in women undergoing their first laparoscopy for the investigation of pelvic pain, how many women do in fact have tenderness and tension in their pelvic floor muscles and whether this is associated with their pelvic pain.

We will also investigate if the pelvic floor muscle tenderness and tension, as well as women's pelvic pain, change following the laparoscopy, in the short term (3 months) and the medium term (1 year).

A sub-study within this study will also test how well gynaecologists and physiotherapists are able to detect pelvic floor muscle tenderness and tension, so that clinicians can better identify which women may have these pelvic floor muscle problems and receive appropriate treatment.

Are you interested? Are you eligible to participate in this project?

If you are planning to have a laparoscopy (key hole surgery) for pelvic pain, you may be eligible.

What happens if I participate in this project?

You will be asked to have an extra visit before your surgery for a physiotherapy assessment of your pelvic floor muscles.

You will be asked to answer an online questionnaire before your laparoscopy and the findings at your surgery will be recorded.

Further online questionnaires and extra physiotherapy visits at 3 months and 12 months after surgery are required.

A modest-value retail voucher reimbursement will be given for your time and travel. In addition, one of the tools used to measure your pelvic floor muscles, called a 'Femfit', will be given to you to keep for your future use – you may find this helpful for your pelvic floor muscles (more details will be given and explained after you enter this project).

Project 8:

Assessing change in Anti-Mullerian Hormone (ovarian reserve) associated with surgical excision vs conservative management of endometrioma: A longitudinal cohort study

Endometriomas are benign cysts of the ovary that occur in women with endometriosis. These women also have an increased risk of infertility and therefore can require medical treatments in order to conceive. Management of these cysts prior to fertility treatment is controversial. On the one hand, leaving them has the potential for the cyst to get bigger and further damage ovarian tissue including eggs, as well as the rare risks of malignancy and serious infection due to egg collection from the ovaries during fertility treatment. On the other hand, surgically removing the cyst has been shown to decrease the ovarian reserve, or the number of eggs left in the ovary and puts the patient through the risks of surgery.

This study aims to investigate how the ovarian reserve changes over time in women with endometrioma left alone compared to those that have them surgically removed. This will help to decide the best way to manage these cysts in the future where fertility is desired. We plan to measure the ovarian reserve using anti-mullerian hormone which is secreted by the ovary and correlates with the number of follicles available. This is measured by a blood test. The participants in this study will already have a management plan for their endometrioma and we will observe the change in the ovarian reserve by taking blood samples at 7 time points: at recruitment, 6 months post-surgery or recruitment, 12 months post-surgery or recruitment and then again at 2, 3, 4 and 5 years.

These time points will be similar for both groups to ensure comparable times between recruitment and follow-up in both study arms. The results will be available to the participants and any abnormal results will be discussed with them by the investigative team and appropriate referrals made.

Are you interested? Are you eligible to participate in this project?

If you had an ultrasound to show that you have endometriosis cyst (endometrioma) of >2cm in size, you may be eligible.

What happens if I participate in this project?

You will be asked to do online questionnaires and have blood tests done (at your choice of your nearest specified community pathology place) at specified times as described above. You will be informed of the blood test results.

There will be no change to your treatment.

Project 9:

A prospective longitudinal cohort study of the effect of conservative and surgical management for moderate to severe endometriosis on future fertility

Endometriosis is a condition where tissue similar to the lining of the uterus (endometrium) is found developing in other areas of the pelvis. Women who have difficulty becoming pregnant are more likely to have endometriosis. In women with minimal to mild endometriosis, there is evidence that surgery to remove it increases the chance of becoming pregnant naturally. There is, however, no clear evidence about the effect of surgically removing moderate and severe endometriosis on the chance of pregnancy. Many women express a strong desire to protect their future ability to become pregnant. This puts them in a difficult situation if they are diagnosed with endometriosis – do they have it treated surgically, with the associated risks (including loss of healthy ovary tissue and/or development of pelvic scar tissue) or do they leave it alone, in which case it might grow and be a greater risk to the possibility of future children?

This study aims to provide clearer information for women with known endometriosis who have already been trying for pregnancy for at least 12 months. It will document their monthly chance of pregnancy from trying naturally and compare this between women who have surgery and those who don't. The same comparison will also be done for women trying for pregnancy through in vitro fertilization (IVF). In addition, this study will assess the effect of watching compared to surgery on future pregnancy in women who are not yet trying to start a family.

Women who enrol in this study will be asked to complete an initial questionnaire and then will complete a short questionnaire (less than 5 minute) each month at the time of their period. This will be undertaken either through an online questionnaire or via a mobile phone app.

Are you interested? Are you eligible to participate in this project?

If you have known moderate to severe endometriosis (either based on ultrasound or previous surgery findings) and you desire fertility (now or in the future), you may be eligible

What happens if I participate in this project?

You will be asked to do online questionnaires as specified above.

There will be no change to your treatment and there will be no extra visits.

Further Information:

Your doctor is likely to briefly mention some of these important research projects to you during the course of your consultation. Depending on your eligibility, a member of the research team may contact you to further discuss your interest in one or more of the projects.

You can read more information on this research by visiting our website: [URL to be confirmed]. Contact details for the project coordinators are also available on this website.

If you are interested or would like to know more about our research, please contact our research team and email your details to: Endo-Research@unimelb.edu.au

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