Light at the end of the tunnel

Molecular imaging agent is studied in endometriosis

The World Health Organization has described endometriosis as one of the most pernicious conditions affecting women of childbearing age because of its painful symptoms and its potential to lead to infertility. An estimated 10% of women of reproductive age are affected by the condition which can start at a person's first menstrual period and last until menopause. The disease is characterised by the growth of tissue similar to the lining of the uterus outside the uterus. This leads to inflammation and scar tissue forming in the pelvic region and sometimes elsewhere in the body.

The pain caused by the condition is compounded by uncertainty involving its diagnosis. According to the US Mayo Clinic, pelvic pain associated with endometriosis can be confused with pelvic inflammatory disease or ovarian cysts. Or it can be mistaken for irritable bowel syndrome which can cause stomach cramps.

However the sheer number of women affected has triggered more research with the result that some scientists are suggesting that endometriosis may be not one disease but a group of disease subtypes amenable to molecular profiling, according to a paper in *Nature Medicine*[1]. This brings the issue of diagnosis to the forefront, even as there is an ongoing debate about the cause of the disease. The current diagnostic standard for endometriosis is laparoscopic surgery, an invasive procedure.

In January, the first non-invasive diagnostic test for endometriosis was launched in several European countries following its approval by the French National Authority of Health. Developed by the French company Ziwig SAS, the test is a saliva-based microRNA signature for endometriosis. Ziwig was awarded the Prix Galien in France for its work. But sceptics abound, arguing that more work needs to be done to verify the Ziwig test results.

Amidst all of this activity, Serac Healthcare Ltd, a nuclear medicine company, has been quietly working on a molecular imaging agent that it says will be able to diagnose endometriosis at the earliest stage. This is peritoneal endometriosis when endometrial-like tissue first develops along the lining of the abdominal cavity. Serac Healthcare is a wholly owned subsidiary of Serac Life Sciences Ltd, a private limited company located in the UK. In 2018, Serac Healthcare acquired the molecular imaging agent maraciclatide from GE Healthcare. Maraciclatide is being evaluated as a potential diagnostic for both inflammatory arthritis and endometriosis.

In an interview David Hail, the Serac Healthcare chief executive, explained the strategy for maraciclatide and commented on preliminary findings of a Phase 2 study in endometriosis. "Our focus is on providing a definitive non-invasive diagnostic test, a quick test, at the earliest stage of endometriosis where there is the possibility to intervene and change the course of the disease," he said.

99mTc-maraciclatide is a radiolabelled peptide that binds to integrin receptors on cells that are upregulated in diseases involving angiogenesis and inflammation. The molecule is synthetic and has been shown to bind specifically to alpha v beta 3 integrin receptors. The molecule includes a chelator for radiolabelling. In this case, the radionuclide is technetium-99m which has been approved by the US Food and Drug Administration for the diagnostic imaging of multiple organs in the body. The molecule is administered intravenously – thus non-invasive – by gamma scintigraphy or SPECT-CT (single photon emission computed tomography scan with computed tomography). A Phase 1 study conducted in 2003 concluded that the agent was safe with a dosimetry, or radiation exposure, similar to other 99m-Tc-based imaging agents.

Preliminary data from a Phase 2 study of the imaging agent were released on 15 March at a meeting of the Society for Reproductive Investigation in Vancouver, Canada. The gap in time between the Phase 1 and Phase 2 studies is explained by the fact that ownership of the maraciclatide molecule changed hands during this period, according to Serac.

The data showed that 99mTc-maraciclatide was able to visualise superficial peritoneal endometriosis which is found in the thin peritoneum lining which covers the abdomen and pelvis. Currently, this can only be identified accurately by surgery. This subtype accounts for about 80% of all endometriosis diagnoses. In the study, the imaging agent correctly identified superficial peritoneal endometriosis in patients who went on to have early-stage endometriosis confirmed by laparoscopic surgery.

In the interview, Mr Hail said that the potential of a non-invasive diagnostic test that could demonstrate the extent and location of endometrial growth outside the uterus in a timely way was enormous. In the diagnostic field this could mean "many, many more women getting an appropriate diagnosis."

The Phase 2 study, which is being sponsored by the Oxford Endometriosis Care Centre and the Nuffield Department of Women's and Reproductive Health, Oxford University, UK, is expected to complete before the end of the year. The next step will involve opening discussions with the FDA ahead of starting a Phase 3 trial for 99mTc-maraciclatide. Under FDA guidance, imaging agents are generally governed by the same rules as drug and biological products. However because they are only used for diagnosis, the development plans for these agents can be tailored to reflect these uses.

"The prospect of women being able to make earlier or better decisions for themselves and for clinicians to make better decisions is a huge unmet medical need at the moment. And to be honest with you, that's good enough to start the day," Mr Hail said.

Reference: 1. Watson, Clare, Surge in endometriosis research after decades of underfunding could herald new era for women's health, *Nature Medicine*, Volume 30, February 2024.

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