'Toxic' oestrogen by-product linked with fatal lung condition

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(Medical Xpress) -- The breakdown of oestrogen could play an important role in the onset of a rare but devastating condition of high blood pressure in the lungs.

In a study funded by the British Heart Foundation (BHF) and published in American Heart Association journal *Circulation*, scientists from the University of Glasgow showed that high levels of an enzyme in the lungs called CYP1B1 – which breaks down oestrogen into harmful smaller molecules – could play a role in the development of pulmonary arterial hypertension.

Around 3,000 people in the UK have pulmonary arterial hypertension, when overactive cell growth in blood vessel walls reduces the space for blood flow in the lungs. Often affecting younger, pre-menopausal women, symptoms include breathlessness and chest pain. The signs worsen as lung blood pressure increases, and the disorder is often fatal. More than one in ten patients die within the first year of diagnosis.

Although there are treatments available, they are often not effective.

This new study shows a link between high levels of a harmful molecule produced from the breakdown of oestrogen by CYP1B1 and the development of pulmonary arterial hypertension. The findings could help lead to new treatments to tackle the disease.

The researchers showed that CYP1B1 levels were elevated in the lungs

of mice with pulmonary arterial hypertension, and that lowering CYP1B1 levels reduced the severity of the disease. A 'toxic' by-product of oestrogen – called 16α-hydroxyestrone – was found in elevated amounts in the urine of mice that did develop the condition.

Importantly, the researchers also examined a small number of lung samples from human patients with pulmonary hypertension – all of whom had elevated levels of CYP1B1. This means that targeting the enzyme with a specific drug in the future might make a difference for patients.

Professor Mandy MacLean, Professor of Pulmonary Pharmacology at the University of Glasgow's Institute of Cardiovascular and Medical Sciences, who leads a BHF programme grant, said: "Pulmonary arterial hypertension is a really debilitating disease, often fatal, that we need to do more to understand.

"We found that its onset seems to have a lot to do with raised levels of toxic molecules in the lungs, produced from the breakdown of oestrogen by a regulatory protein that's gone out of control.

"We think it's an important discovery because drugs that target this protein – called CYP1B1 – already exist, so our discovery provides a real rationale to go on to test these drugs in human patients."

Dr Shannon Amoils, Research Advisor at the BHF, which co-funded the research, said: "Pulmonary arterial hypertension is more common in women, which has led to the suggestion that the higher oestrogen levels found in women might be linked to higher risk. Up till now, though, studies in animal models haven't come up with a clear answer.

"This interesting study in mice, which also looked at human samples, shows that abnormal oestrogen breakdown in the lungs may be an

important factor. But many questions about this condition are still unanswered, and the next stage is to move on to examine this association more closely in patients."

Provided by University of Glasgow

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