

FOCUS ON RESEARCH

VASCULAR FUNCTION IN COPD: MECHANISMS FOR INCREASED CARDIOVASCULAR RISK

Dr J Maclay, Dr D McAllister, Dr N Mills, Dr J Miller, Professor D Newby and Professor W MacNee

Aim

To perform comprehensive studies of vascular function in patients with chronic obstructive pulmonary disease (COPD – a smoking related lung disease) and controls matched for age, sex and smoking history in order to determine mechanisms of the increased risk of heart attacks and strokes associated with COPD.

Project Outline/Methodology

We measured arterial stiffness, a recognised risk factor for coronary artery disease, by assessing the form of the pulse wave in 102 patients with COPD and 103 healthy controls matched for age and smoking status. In a second study of 157 patients with COPD, we measured pulse wave velocity (a validated measure of arterial stiffness) by measuring the velocity of the pulse wave from the carotid to the femoral pulse and in addition we assessed emphysema (destruction of the lungs in COPD patients) using computed tomography (CT) imaging in a subgroup of 73 patients.

In a third study we performed comprehensive assessment of blood vessel function in 18 men with COPD and 17 healthy male control subjects, matched for age and smoking history and no history of heart disease, diabetes or other conditions known to affect vascular function. Arterial stiffness was measured both by analysis of the pulse wave and as the pulse wave velocity. We also assessed the function of the lining of the blood vessels (the endothelium). By comparing the relaxation of blood vessels in response to drugs which act directly on the endothelium as well as drugs which bypass the endothelium, it allowed us to establish if the function of the endothelium was impaired. Patients with stiffer arteries and abnormal function of the endothelium have increased risk of heart attack and strokes.

Additionally, we measured endothelial release of tissue plasminogen activator (t-PA) which prevents clot formation. Furthermore we measured markers of platelet activation, which aggregate to form the clots that cause heart attacks.

Key Results

We found that there was no difference between patients with COPD and controls regarding endothelial function. However, patients with COPD had stiffer arteries and more platelet activation than

controls. Arterial stiffness was also related to the extent of emphysema.

Conclusions

Patients with COPD have increased arterial stiffness and platelet activation than age, sex and smoking matched controls. These factors may contribute to the increased risk of heart attacks and strokes associated with this condition. There was no difference in endothelial function between the groups. Arterial stiffness and emphysema are related suggesting shared mechanisms for both conditions.

What does this study add to the field?

Although other groups have shown increased arterial stiffness in COPD, they have not been matched for smoking status. It has been suggested that the stiffer arteries in COPD are due to endothelial dysfunction, but we have shown that this is not the case. Furthermore, we have shown increased platelet activation in COPD, which may contribute to an increased risk of clots in blood vessels that supply the heart. Now that we know that arterial stiffness is not caused by abnormal endothelial function, we wonder if there is an abnormality in the structural proteins that make up the blood vessels, elastin and collagen. These proteins are broken down in the lungs in COPD and finding out if this occurs in the rest of the body may give clues as to the cause of COPD.

Implications for Practice or Policy

The abnormalities that we have found provide potential targets for therapy, directed at trying to improve vascular function in COPD, reducing the risk of heart attacks.

Where to next?

We are keen to look for other evidence of elastin breakdown in another organ that is rich in elastic tissue – the skin. We also want to look for antibodies in individuals with COPD that may target structural proteins throughout the body.

Further details from:

Professor William MacNee,
Queen's Medical Research Institute,
47 Little France Crescent,
Edinburgh, EH16 4TJ.