Fighting cardiovascular disease with knowledge gained from pregnancy

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Early maternal vascular adaptations to pregnancy are paramount to the survival and development of the fetus, and for maternal health. Cardiac output and blood volume increase by 40-50%, whereas peripheral vascular resistance decreases. Global arterial compliance increases in parallel with cardiac output, thereby preserving diastolic pressure. These physiological adaptations are achieved through a number of mechanisms including changes in reactivity to vasoconstrictors and vasodilators, and vascular remodelling. Endothelium-derived mediators of vasodilation, nitric oxide (NO), prostacyclin (PGI2), and endothelium-derived hyperpolarization (EDH) are also up-regulated during pregnancy and contribute to these important vascular adaptations. Failure of the maternal systemic vasculature to adapt sufficiently can lead to serious complications such as pregnancy-induced hypertension and preeclampsia.

The peptide hormone relaxin is widely recognised for mediating the essential renal and systemic hemodynamic adaptations in early pregnancy through direct actions on the maternal vasculature. However, studies in relaxin gene knockout mice identified that endogenous relaxin is not only a ‘pregnancy hormone’ but also has important functions in a number of tissues in males and non-pregnant females, including the cardiovascular system. This led to the idea that treatment with relaxin could improve vascular function in disease conditions characterized by endothelial dysfunction and/or arterial stiffness (Leo *et al.*, 2016). Exogenous relaxin treatment for 2-5 days or acute intravenous injection can rapidly enhance endothelium-dependent vasorelaxation and decrease myogenic reactivity. This vascular response to relaxin is prolonged even in the absence of circulating relaxin and is tightly regulated by the production of endothelium-derived relaxing factors including NO, EDH and PGI2 at least in mesenteric arteries. But relaxin has a broader range of biological actions including anti-oxidant and anti-inflammatory effects, suggesting it acts as a vasoprotective molecule limiting the damage inflicted by disease. There is also evidence that relaxin can remodel the vasculature and improve arterial compliance, particularly under disease conditions. Thus, relaxin is clearly differentiated from other vasodilator drugs and has the potential to be used as a therapeutic in many cardiovascular diseases *e.g.* heart failure, diabetes, preeclampsia, either alone or in combination with standard therapy.

Leo CH, Jelinic M, Ng HH, Tare M, Parry LJ. (2016). Serelaxin: a novel therapeutic for vascular diseases. *Trends Pharmacol Sci* **37(6)**, 498-507.