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The *in vitro* effect of commonly used pharmacological agents on small human pulmonary arteries

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Background: Acute pulmonary hypertension following cardiac surgery can have a significant effect on postoperative morbidity and mortality. Phosphodiesterase inhibitors, nitric oxide and prostacyclin analogues are commonly used to treat acute pulmonary hypertension. In recent years our group has used human pulmonary artery rings in an *in vitro* model to investigate pulmonary vascular resistance. The aim of this study was to characterize the pharmacological effects of clinically used vasodilators on the human pulmonary vasculature in comparison to the endogenous pulmonary vasodilators, atrial natriuretic peptide and brain natriuretic peptide.

Methods: 35 pulmonary artery rings of internal diameter 2-4 mm and 2 mm long, mounted in a multi-wire myo-graph system, were used for measuring changes in isometric tension. After preconstruction with PGF₂ α (11 μ M) concentration response curves were constructed to sildenafil (Sd), milrinone (Mi), sodium nitroprusside (SNP), atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), epoprostenol (Ep) and iloprost (Ip) by cumulative addition to the myo-graph chambers.

Results: Sd, Mi, SNP, ANP, BNP, Ep and Ip caused concentration-dependent vasodilation in the pulmonary arteries (EC₅₀ 1.06 μ M, 1.01 μ M, 22.6 nM, 1.11 nM, 28.78 nM, 29.40 nM and 1.43 nM respectively). The order of efficacy was ANP=Ep=Ip=Mi > SNP > Sd > BNP and the order of potency was ANP>Ip>SNP>BNP=Ep>Mi=Sd.

Conclusion: This is the first study to demonstrate the differential *in vitro* effects of clinically used pulmonary vasodilators and endogenous vasodilators on small human pulmonary vessels. ANP was the most potent and effective vasodilator whereas BNP had little effect. The prostacyclin analogues and milrinone had similar efficacy to ANP in small human pulmonary arteries. BNP could be acting as a partial agonist in small human PAs and in subsequent studies BNP was found to inhibit relaxation to ANP, which could have significant implications in decompensated heart failure.

Biography

Azar Hussain is a Cardiothoracic Surgeon with particular interest in Pulmonary Hypertension and Heart Failure. He recently completed his MSc in Translational Research at University of Bristol and currently, pursuing his MD. He is a HYMS Clinical Research Fellow in Department of Cardiothoracic Surgery at Castle Hill Hospital working with Prof Alyn Morice and Prof Mahmoud Loubani was awarded two prizes at the International Conference on Cardiovascular Medicine held in August 2016. He won the best Young Researchers Forum award and the best Poster Presentation award in recognition of his research on "Pulmonary arteries, constrictors and dilators" that have clinical implications for the treatment of patients with pulmonary hypertension in general but more specifically in patients undergoing complex heart surgery.

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