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Sildenafil (Viagra), hemodynamics and the lung

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Keywords

Phosphodiesterase inhibitors, pulmonary circulation, vasodilator therapy

Context

Pulmonary hypertension (PHT) is a disease that carries a high mortality. The only presently available treatments apart from administration of oxygen, are nitric oxide administration and lung transplantation. Vasodilators (for example calcium channel blockers) are not selective for the pulmonary circulation, as they lower mean pulmonary arterial pressure (MPAP), mean systemic arterial pressure (MAP), and cardiac output (CO).

The aims of this study were to examine the effects of sildenafil (Viagraa) on hemodynamics and pulmonary gas exchange in a porcine model. Sildenafil is a selective oral phosphodiesterase-V (PDE-V) inhibitor and is presently used to treat male impotence. PDE-V is present in high concentrations not only in the corpora cavernosa, but also in vascular, tracheal and visceral smooth muscles. Inhibition of this enzyme leads to increased cGMP, which results in vascular relaxation. Dipyridamole is also an inhibitor of PDE-V, albeit a nonselective one.

Significant findings

Low normal and high doses (25, 50 and 100 mg respectively) of sildenafil depressed the partial pressure of arterial oxygen PaO_2 most likely through increased intrapulmonary shunt flow. CO was increased, MAP was reduced, and MPAP decreased after high dose (100 mg).

Comments

This class of drug may represent a novel way to augment CO and reduce MPAP. However the decrease in PaO_2 is worrisome. Limitations of this study include the fact that oral administration in anesthetized animals could result in possible variable absorption of the drug. An intravenous infusion is more likely to standardize serum levels, but the drug is not available in this form. While the porcine cardiopulmonary system is very similar to that of humans, there are clearly differences between this anesthetized ventilated model, and awake patients. Moreover, these were swine that did not have evidence of elevated MPAP.

The etiology of PHT is multifactorial. Patients with elevated MPAP secondary to acute respiratory distress syndrome differ from those with elevated MPAP due to sleep apnea. Thus, if a drug is beneficial in one circumstance, it may not necessarily be beneficial in another. Nevertheless, sildenafil probably represents only the first of what is likely to become a new class of pulmonary vasodilators. Additionally, the effect of augmenting CO may also have therapeutic implications. Clearly much work remains to be done on PDE inhibitors. Such further information may lead to better treatment modalities, and more importantly, a clearer understanding of the pathophysiology of PHT.

Methods

Porcine model, nasogastric administration, hemodynamic measurements, multiple inert gas elimination technique

Additional information

References

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