Abstract
Chronic damage to pulmonary vessels leads to pulmonary hypertension (PH). Different forms of PH are quite frequent and are associated with significant morbidity and mortality. The treatment of PH is most successful, if its cause can be identified and removed before irreversible damage to the pulmonary vascular bed occurs. For patients, in whom the elimination of the underlying cause is not possible or where the cause is unknown, the treatment is aimed at reduction of pulmonary vascular resistance and improvement of cardiac and circulatory response to pressure overload of the right ventricle. One option for the PH treatment is modification of metabolism of cyclic guanosine monophosphate (GMP), which is the second messenger of nitric oxide and induces vascular vasodilation. Cyclic GMP is degraded by phosphodiesterases (PDE 5).
In the clinical part, we tested the hypothesis that acute inhibition of PDE5 by sildenafil provides more selective pulmonary vasodilation than high doses of prostaglandin E1 (PGE1). The study showed that the vasodilator effects of sildenafil on pulmonary circulation is more pronounced than in the systemic circulation and that sildenafil had a greater ability to detect reversible component precapillary PH due to advanced chronic heart failure than PGE1.
The aim of our experimental work was to test the hypothesis that chronic administration of a combination of L-arginine, which is a precursor of nitric oxide, and sildenafil brings an additive effect on hemodynamic parameters in a pulmonary circulation, remodeling of pulmonary arterioles and right ventricular hypertrophy in animal models of hypoxic PH. Our study demonstrated a beneficial effect of combined administration of L-arginine and sildenafil as they lowered pulmonary artery pressures and decreased the peripheral pulmonary vascular remodeling. Combined administration of L-arginine, and sildenafil was better than only the use of sildenafil alone or L-arginine, because there was additional effect of intracellular cyclic GMP due to increased production and inhibition of its degradation.