

ABSTRACT

Comparative Effects of Ketamine and Propofol on Vascular Reactivity in Streptozotocin (STZ)-Induced Diabetic Rats

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Diabetes is an independent and major risk factor for the development of vascular complications due to endothelial and potassium ion channel dysfunction, thereby causing hemodynamic instability. This increases the risk of peri-operative morbidity and mortality in affected individuals. Anaesthetic agents also alter the hemodynamics during surgery in normal healthy subjects which is further compromised in diabetic patients. This study compared the vascular response of aortic rings isolated from streptozotocin (50mg/kg)-induced Type 1 DM and non-DM (control) rats to ketamine and propofol, and in the presence and absence of potassium channel modulators. An organ bath set-up was used to ascertain contractions to phenylephrine (10^{-10} - 10^{-4} M) and relaxation to acetylcholine (10^{-10} - 10^{-4} M), ketamine (10^{-9} - 10^{-1} M) and propofol (10^{-9} - 10^{-1} M) following pre-contraction with phenylephrine (10^{-6} M) in the presence and absence of potassium channel modulators. The modulators included: barium chloride (inward rectifying potassium channel [Kir] blocker, 10^{-4} M); 4-aminopyridine (voltage-gated potassium channel [Kv] blocker, 10^{-3} M); glibenclamide (ATP-sensitive potassium channel [K_{ATP}] blocker, 10^{-5} M); tetraethylammonium (large calcium potassium channel [BK_{Ca}] blocker, 10^{-3} M); NS1619 (BK_{Ca} potassium channel opener, 10^{-7} M) and nicorandil (ATP-sensitive and Kir potassium channel opener,

10^{-6} M). Contraction to phenylephrine was significantly enhanced ($f=30.157^b$, $p<0.001$) and relaxation to acetylcholine was significantly reduced ($f=23.887^b$, $p<0.05$) in diabetic rats versus control. Ketamine-induced relaxation was significantly ($F=32$, $p<0.05$) enhanced in the presence of glibenclamide while propofol-induced relaxation was significantly ($p=0.032$) attenuated in diabetic rats versus control. Activation of potassium channels with nicorandil and NS1619 did not alter the vascular response to ketamine or propofol in diabetic aortic rings when compared to control. The results suggest that endothelial-dependent relaxation and vascular contraction are impaired in DM. Following inhibition of K_{ATP} channels, the relaxation response to ketamine was increased but was decreased to propofol. Inhibition of Kir channels attenuated the vascular relaxation response to propofol but did not alter the response to ketamine while inhibition of Kv channels decreased the vascular response to ketamine and propofol. Activation of K_{ATP} , Kir and BK_{Ca} did not alter ketamine or propofol-induced relaxation.

Keywords: Joan Elizabeth Facey, Aorta, Diabetes Mellitus, Ketamine, Propofol and Potassium Channel Modulators.