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A systematic review and meta-analysis of the haemodynamic effects of Δ^9-Tetrahydrocannabinol *in vivo* in animals and humans

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Introduction: The effects of Δ^9-Tetrahydrocannabinol (THC) on the cardiovascular system are complex. The aim of the present study was to systematically review and analyse *in vivo* studies evaluating the effects of THC on haemodynamics.

Methods: PubMed, Medline and EMBASE were systematically reviewed for studies assessing the haemodynamic effects of THC. Pre-specified inclusion criteria was used to prevent bias: studies had to be *in vivo*; assess at least one of blood pressure (BP), heart rate (HR) or blood flow (BF); be an original article and a controlled study; and include cannabis naïve subjects. Changes in BP (mmHg), HR (beats per minute, bpm) and BF (percentage change or mL/min) at 2 hours post-single (acute) dose, or after repeated (chronic) dosing, were extracted and analysed using Cochrane Review Manager software.

Results: Thirty-one studies assessing the haemodynamic effects of THC met the eligibility criteria. Fourteen publications assessed BP (n=541) and twenty-two assessed HR (n=567) among six species. Three publications assessed BF in two species (n=45). Acute THC dosing significantly reduced BP and HR in anaesthetised animals (BP, mean difference (MD) -19.7 mmHg, 95% CI -26.16, -13.25, p<0.00001; HR, MD −53.49 bpm, 95% CI -65.9, -41.07, p<0.00001), conscious animals (BP, MD -12.3 mmHg, 95% CI -19.42, -5.18, p=0.0007; HR, MD −30.05 bpm, 95% CI -38.47, -21.64, p < 0.00001), animal models of stress or hypertension (BP, MD -61.37 mmHg, 95% CI -117.56, -5.17, p=0.03), and significantly increased cerebral blood flow (CBF) in murine stroke models (MD 32.35%, 95% CI 23.81, 40.88, p<0.00001). Chronic dosing increased BF (MD 21.95 mL/min, 95% CI -0.38, 44.29, p=0.05) in anaesthetised animals and reduced BP in animal models of stress or hypertension (MD -22.09 mmHg, 95% CI -30.61 mmHg, -13.58, p<0.00001). In humans, acute THC dosing significantly increased HR (MD 8.16 bpm, 95% CI 4.99, 11.33, p<0.00001). Species, experimental conditions (anaesthetised, conscious, stress or hypertensive) and dose all affected haemodynamic responses to THC. Statistical heterogeneity was present among analyses of BP and HR post-acute THC dosing in animals and humans (p<0.00001), and in BP post-chronic THC dosing in anaesthetised animals (p=0.03).

Conclusion: Haemodynamic responses to THC varied according to species (tachycardia in humans; bradycardia, hypotension and increased BF in animals), experimental conditions and dose. Data in humans are largely limited to responses in HR warranting further investigation.