Review Article

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Cannabinoids in experimental stroke: a systematic review and meta-analysis

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Cannabinoids (CBs) show promise as neuroprotectants with some agents already licensed in humans for other conditions. We systematically reviewed CBs in preclinical stroke to guide further experimental protocols. We selected controlled studies assessing acute administration of CBs for experimental stroke, identified through systematic searches. Data were extracted on lesion volume, outcome and quality, and analyzed using random effect models. Results are expressed as standardized mean difference (SMD) with 95% confidence intervals (CIs). In all, 144 experiments (34 publications) assessed CBs on infarct volume in 1,473 animals. Cannabinoids reduced infarct volume in transient (SMD −1.41 (95% CI −1.71), −1.11) P<0.00001) and permanent (−1.67 (−2.08, −1.27), P<0.00001) ischemia and in all subclasses: endocannabinoids (−1.72 (−2.62, −0.82), P=0.0002), CB_1/CB_2 ligands (−1.75 (−2.19, −1.31), P<0.00001), CB_2 ligands (−1.65 (−2.09, −1.22), P<0.00001), cannabidiol (−1.20 (−1.63, −0.77), P<0.00001), Δ^9-tetrahydrocannabinol (−1.43 (−2.01,

−0.86), P<0.00001), and HU-211 (−2.90 (−4.24, −1.56), P<0.0001). Early and late neuroscores significantly improved with CB use (−1.27 (−1.58, −0.95), P<0.00001; −1.63 (−2.64, −0.62), P<0.002 respectively) and there was no effect on survival. Statistical heterogeneity and publication bias was present, median study quality was 4 (range 1 to 6/8). Overall, CBs significantly reduced infarct volume and improve functional outcome in experimental stroke. Further studies in aged, female and larger animals, with other co-morbidities are required.

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