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

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Background

Cannabinoids (CB) (including endo-, phyto- and synthetic -CBs) show promise as a neuroprotective treatment for stroke, with some agents already licensed, and well tolerated, in humans for other conditions. We aimed to systematically review and meta-analyse the use of CBs in experimental stroke.

Methods

Relevant studies were identified with searches of Medline, Embase and PubMed. Data was extracted on stroke lesion volume, neurological outcome and methodological quality. Data were analysed using Cochrane Review Manager using random effects models; results are expressed as standardised mean difference (SMD) with 95% confidence intervals [CI].

Results

94 studies from 22 publications assessed the effect of CBs on infarct volume in a total of 1022 male animals (512 rats, 496 mice, and 14 monkeys). CBs reduced infarct volume significantly in transient (SMD -1.26, [95% CI -1.53, -0.99], $p<0.00001$) and permanent (SMD -2.22 [-2.88, -1.56] $p<0.00001$) models of ischaemia and in all subclasses of CBs analysed: endocannabinoids (SMD -0.71 [-1.22, -0.21]), CB_1/CB_2 receptor ligands (SMD -1.76 [-2.36, -1.17]), CB_2 ligands (SMD -1.64 [-2.08, -1.21]), cannabidiol (SMD -1.05 [-1.50, -0.59]), tetrahydrocannabinol (SMD -1.43 [-2.01, -0.86]) and HU-211 (SMD -3.73 [-5.86, -1.60]). Significant statistical heterogeneity was present ($p<0.00001$) and median study quality was 4 (range 2-6/8). Data on neurological outcome will also be presented.

Conclusions

CBs significantly reduce infarct volume in experimental stroke. Systematic review revealed that further studies in aged, larger and female animals models, with other co-morbidities (hypertension, diabetes) are required.