LOCAL ADMINISTRATION OF PALMITOYLETHANOLAMIDE REDUCES CHRONIC GRANULOMA-ASSOCIATED ANGIOGENESIS IN RAT

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Chronic inflammation is often associated to granuloma formation that is an hallmark of many human diseases. Cannabinoids exert a large number of biological effects through the interaction with two G protein-coupled receptors normally binding endogenous ligands, as anandamide and 2-arachidonoyl glycerol. Other putative endocannabinoids, as palmithoylethanolamine (PEA) has been identified. PEA is an "atypical" endocannabinoid because it exerts different endocannabinoid-like pharmacological activities including anti-inflammatory and analgesic activity in neuropathic pain without any cannabinoid receptor binding. Mechanism of action of PEA is a puzzling, in fact although this compound does not bind with high affinity to CB1 and CB2 receptors, it exhibits some cannabinoid-mimetic actions which could be explained at least in part by entourage effects. PEA has been proposed to act as "ALIAmide" (Autacoid Local Inflammation Antagonist Amide) and it has been proposed to have potent anti-inflammatory and antioxidant activity by modulating mast-cell degranulation. Therefore, aim of our study was to investigate whether PEA modulates λ-carrageenin-induced granuloma formation and the release of several pro-inflammatory and pro-angiogenic mediators at 96 h in rats. Our results demonstrate that local administration of 100μL of PEA (200-400-800 mg/ml) was effective in strongly reducing granuloma weight in a dose-related fashion. Moreover, the administration of PEA was able to reduce new vessels formation in granulomatous tissue evaluated both by haemoglobin content and TNF-α and chymase protein expression, two mediators that are present in mast cell granules.
In conclusion our study demonstrate that PEA is able to reduce chronic inflammatory process, at least in part, through the modulation of the mast cells activation, which play a pivotal role during inflammatory scenario.