Abstract

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Anti-proliferative and apoptotic effects of anandamide in human prostatic cancer cell lines: implication of epidermal growth factor receptor down-regulation and ceramide production.

Mimeault M[1], Pommery N, Wattez N, Bailly C, Hénichart JP.

Author information

Abstract

BACKGROUND: Anandamide (ANA) is an endogenous lipid which acts as a cannabinoid receptor ligand and with potent anticarcinogenic activity in several cancer cell types.

METHODS: The inhibitory effect of ANA on the epidermal growth factor receptor (EGFR) levels expressed on the EGF-stimulated prostatic cancer cells LNCaP, DU145, and PC3 was estimated by ELISA tests. The anti-proliferative and cytotoxic effects of ANA were also evaluated on these human prostatic cancer cell lines by growth tests, flow cytometric analyses, trypan blue dye exclusion assays combined with the Papanicolaou cytological staining method.

RESULTS: ANA induced a decrease of EGFR levels on LNCaP, DU145, and PC3 prostatic cancer cells by acting through cannabinoid CB(1) receptor subtype and this leaded to an inhibition of the EGF-stimulated growth of these cells. Moreover, the G(1) arrest of metastatic DU145 and PC3 growth was accompanied by a massive cell death by apoptosis and/or necrosis while LNCaP cells were less sensitive to cytotoxic effects of ANA. The apoptotic/necrotic responses induced by ANA on these prostatic cancer cells were also potentiated by the acidic ceramidase inhibitor, N-oleoylethanolamine and partially inhibited by the specific ceramide synthetase inhibitor, fumonisin B1 indicating that these cytotoxic actions of ANA might be induced via the cellular ceramide production.

CONCLUSIONS: The potent anti-proliferative and cytotoxic effects of ANA on metastatic prostatic cancer cells might provide basis for the design of new therapeutic agents for effective treatment of recurrent and invasive prostatic cancers.

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