Cannabinoids in pancreatic cancer: correlation with survival and pain.

Cannabinoids exert antiproliferative properties in a variety of malignant tumors, including pancreatic ductal adenocarcinoma (PDAC). In our study, we quantitatively evaluated the immunoreactivity for cannabinoid-1 (CB1) and cannabinoid-2 (CB2) receptors as well as for the endocannabinoid metabolizing enzymes fatty acid amide hydrolase (FAAH) and monoacyl glycerol lipase (MGLL). Furthermore, quantitative real-time RT-PCR for CB1, CB2, FAAH and MGLL in normal pancreas and pancreatic cancer tissues was performed. Levels of endocannabinoids were determined by liquid chromatography/mass spectrometry. Immunoreactivity scores and QRT-PCR expression levels were correlated with the clinico-pathological (TNM, survival, pain) status of the patients. Evaluation of endocannabinoid levels revealed that these remained unchanged in PDAC compared to the normal pancreas. Patients with high CB1 receptor levels in enlarged nerves in PDAC had a lower combined pain score (intensity, frequency, duration; \( p = 0.012 \)). There was a significant relationship between low CB1 receptor immunoreactivity or mRNA expression levels (\( p = 0.0011 \) and \( p = 0.026 \), respectively), or high FAAH and MGLL cancer cell immunoreactivity (\( p = 0.036 \) and \( p = 0.017 \), respectively) and longer survival of PDAC patients. These results are underlined by a significant correlation of high pain scores and
increased survival (p = 0.0343). CB2 receptor immunoreactivity, CB2 receptor, FAAH and MGLL mRNA expression levels did not correlate with survival. Therefore, changes in the levels of endocannabinoid metabolizing enzymes and cannabinoid receptors on pancreatic cancer cells may affect prognosis and pain status of PDAC patients.