PTH-111

DIFFERENTIAL EFFECTS OF SOMATOSTATIN ON TNF RECEPTORS AND APOPTOSIS IN HEPATOCELLULAR CARCINOMA CELL LINES

doi:10.1136/gut.2011.239301.512

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Introduction Somatostatin has antitumour activity in animal models of hepatocellular carcinoma. In human studies both favourable and unfavourable results have been reported. A 40% fraction of treated patients are benefited. Since its action may be through apoptosis, the authors tested the hypothesis that somatostatin may act differently in different hepatocellular cell lines.

Methods The somatostatin synthetic analogue octreotide was tested for its effect on the expression of TNF receptors (RT-PCR and Western blot) and the TNFα-induced apoptosis (NF-kB nuclear translocation, P65 phosphorylation, DNA fragmentation and TUNEL cytochemistry) The HepG2 human hepatoblastoma cells and the Hep3B human hepatocellular carcinoma cells were used.

Results TNFR1 but no TNFR2 receptor was constitutively expressed in both cell lines. Octreotide caused an early (within 1 h) reduction of both mRNA and TNFR1 protein in HepG2 and a late (at 6 and 12 h) reduction in Hep3B cells.

TNFα induced NF-kB nuclear translocation, stronger in Hep3B which was not influenced by octreotide. Octreotide significantly increased P65Ser536 and P65Ser468 phosphorylation, more pronounced in Hep3B cells. Octreotide significantly decreased TNFα-induced Ser536 phosphorylation only in HepG2 cells.

Octreotide or TNFα alone had no effect on apoptosis in HepG2 cells but TNFα greatly increased apoptosis in Hep3B cells. Co-incubation with Octreotide and TNFα increased apoptosis in HepG2 cells and decreased TNFα induced apoptosis in Hep3B cells,

Conclusion (1) The differential effect of somatostatin on apoptosis may be due to its different effect on TNFR1 expression in the two cell lines. (2) Somatostatin may have no direct effect on apoptosis but it may indirectly act through TNF induced apoptosis. (3) This differential effect may in part explain the conflicting results of human HCC studies.

Competing interests None.

Keywords hepatocellular carcinoma, somatostatin, TNF receptors, TNFα.