Role of Fentanyl in Hepatocyte Apoptosis and HCV Infection

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Introduction: In addition to the significant morbidity and mortality directly related to opioid addition/overdose, injection opioid use has led to an increase in the incidence of hepatitis C virus infections (HCV). Although the analgesic effects of opioids via the μ-receptor have been studied, other cellular effects remain unknown. It has been shown that opioids can induce apoptosis in a variety of cell lines. In addition, the pathogenesis of HCV-induced hepatitis involves a balance of pro- and anti-apoptotic mechanisms in hepatocytes. The goal of this study was to investigate the effect of Fentanyl, a synthetic opioid, on hepatocyte viability in conjunction with HCV infection.

Hypothesis: Fentanyl promotes hepatocyte apoptosis and decreased cell viability in vitro. These cytotoxic effects increase when hepatocytes are incubated with HCV E2 (envelope) protein. Fentanyl induces apoptosis via μ-receptor, which can be reversed by the administration of naloxone, a μ-receptor antagonist.

Methods: The presence of μ-receptor in two human hepatocyte cell lines (Huh7 and Huh7.5) was first confirmed by gel electrophoresis and ELISA assay. Hepatocyte cell lines were then grown and incubated 24 hours with administration of Fentanyl 10 ng/ml and/or E2 protein at 1 μg/ml or 100 ng/ml. Control cells were not administered drug/viral protein. E2 was used to mimic cellular response to HCV infection. MTT was used to measure cell viability, and M30 was used to quantify apoptotic levels at 24 hours post-drug/viral protein administration.

Results: Huh7s exposed to Fentanyl demonstrated increased apoptosis and decreased cell viability compared to control cells. Levels of apoptosis increased and cell viability decreased in Huh7s exposed to both E2 and Fentanyl compared to Huh7s exposed to E2 alone.

Conclusions: Fentanyl appears to have cytotoxic effects on hepatocytes and worsens cell viability in the presence of the viral E2 protein. This study can help elucidate the pathogenesis of hepatitis in HCV infection and the risks of accelerated hepatitis associated with drug abuse. Further work will involve repeating measurements of apoptosis and cell viability to Fentanyl and E2 in a dose-dependent manner and administering naloxone to confirm the role of μ-receptor in Fentanyl-induced apoptosis.

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