Protective Effect of Ursodeoxycholic acid in the Chemotherapy Induced Mucositis

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Introduction: Gastrointestinal mucositis is one of the serious side effect of chemotherapy. It causes dose reduction during chemotherapy and increases the frequency of infection, bleeding risk and length of hospitalization. Ursodeoxycholic acid (UDCA) which is currently being used in a wide variety of liver diseases have also direct cytoprotective effects by stabilizing membranes, inhibiting apoptosis, and acting as an antioxidant. We aimed to assess the protective effect of UDCA in chemotherapy induced mucositis in vivo animal model.

Methods: Female Sprague-Dawley rats were randomly allocated to one of the following five groups, non-chemotherapy and vehicle; 5-fluorouracil (5-FU) and vehicle; 5-FU and 10mg/kg/d UDCA; 5-FU and 100mg/kg/d UDCA; 5-FU and 500mg/kg/d UDCA. Intra-peritoneal injection of 5-FU (400mg/kg) or saline (control) was performed. For 5 days, UDCA were administrated orally, starting 1 days before the 5-FU injection. One day after last UDCA administration, rats were sacrificed and dissected the intestines for tissue sample. Laboratory tests were performed.

Results: The protective effect of UDCA was evidenced, among others, by a higher body weight recovery, decreased villus destruction, and reduced inflammatory cytokines. This occurred at doses of 10 and 100mg/kg/day. Villous fusion and destruction were dominant in 5-FU group, compared with UDCA treated group or controls. Jejunal villous lengths of each group were measured; 212.8 ± 58.0 um in 5-FU and vehicle, 331.3 ± 18.0 um in 5-FU and UDCA 10mg/kg, and 310.0 ± 112.6 um in 5-FU and UDCA 100mg/kg. In real time RT-PCR, IL-6 and TNF-a level were decreased in the UDCA 10mg/kg, 100mg/kg co-administration group. Myeloperoxidase activity was decreased in the UDCA co-administration group.

Conclusion: UDCA significantly alleviated the decrease of small intestinal villus height and reduced inflammatory cytokine levels. These results may suggest the potential use of UDCA at appropriate dose as a preventive agent for chemotherapy induced gastrointestinal mucositis. Further studies are needed to define specific mechanisms of protective effect of UDCA on gastrointestinal tract.