13. Prophylactic oral administration of magnesium ameliorates dextran sulfate sodium-induced colitis in mice

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Objective

The number of patients with colitis has been increasing annually. Recently, intestinal inflammation, as one of the factors for its onset, has been demonstrated to be induced by P2X7 receptor-mediated activation of colonic immune cells such as mast cells. Activation of P2X7 receptor (P2X7R) is known to be inhibited by divalent metal cations (DMCs) such as magnesium, but whether or not magnesium administration prevents/relieves colitis is unknown so far. Here, we report that oral (*po*) administration of $MgCl_2$ and ingestion of commercially available magnesium-rich refined deep-seawater (RDSW) relieves dextran sulfate sodium (DSS)-induced colitis in mice.

Materials and Methods

P2X7R activity was evaluated as means of YO-PRO-1 dye uptake by the cells constitutively expressing human and mouse P2X7R. Colitis was induced through ingestion of a 3%(w/v) DSS solution *ad libitum* for 10 days. Brilliant blue G (BBG, a P2X7R antagonist), $MgCl_2$ or RDSW was administered *po* to mice *via* gastric intubation once a day or *ad libitum* from a day before DSS administration for 11 times or 11 days, respectively. Colitis symptoms were determined with disease activity index (DAI), macroscopic and histological evaluation. Magnesium concentrations in feces were measured with ICP-MS.

Results

Based on the findings *in vitro* experiments, we chose magnesium as a potent inhibitor for P2X7R among the DMCs examined. DSS-treated mice exhibited a high DAI, a short colon and a high histological score compared to control mice. As BBG (250 mg/kg, *po*), administration of a $MgCl_2$ solution (100 or 500 mg/kg, *po*) and *ad libitum* ingestion of RDSW (212 ppm as magnesium) significantly attenuated the severity of colitis by decreasing the accumulation of P2X7R-immunopositive mast cells in the colon.

Discussion

Prophylactic *po* administration/ingestion of magnesium and RDSW is considered to be partially, but significantly, effective to protect mice against DSS-induced colitis by inhibiting P2X7R-mediated activation /accumulation of colonic mast cells.