Effect of magnesium supplementation and depletion on the onset and course of acute experimental pancreatitis.

High calcium concentrations are an established risk factor for pancreatitis. We have investigated whether increasing magnesium concentrations affect pathological calcium signals and premature protease activation in pancreatic acini, and whether dietary or intraperitoneal magnesium administration affects the onset and course of experimental pancreatitis. Pancreatic acini were incubated with up to 10 mM magnesium; [Ca(2+)](i) (fura-2AM) and intracellular protease activation (fluorogenic substrates) were determined over 60 min. Wistar rats received chow either supplemented or depleted for magnesium (<300 ppm to 30 000 ppm) over two weeks before pancreatitis induction (intravenous caerulein 10 µg/kg/h/4 h); controls received 1 µg/kg/h caerulein or saline. C57BL6/J mice received four intraperitoneal doses of magnesium (NaCl, Mg(2+) 55 192 or 384 mg/kg bodyweight) over 72 h, then pancreatitis was induced by up to eight hourly supramaximal caerulein applications. Pancreatic enzyme activities, protease activation, morphological changes and the immune response were investigated. Increasing extracellular Mg(2+) concentration significantly...
reduced [Ca(2+)](i) peaks and frequency of [Ca(2+)](i) oscillations as well as intracellular trypsin and elastase activity. Magnesium administration reduced pancreatic enzyme activities, oedema, tissue necrosis and inflammation and somewhat increased Foxp3-positiv T-cells during experimental pancreatitis. Protease activation was found in animals fed magnesium-deficient chow-even with low caerulein concentrations that normally cause no damage. Magnesium supplementation significantly reduces premature protease activation and the severity of pancreatitis, and antagonises pathological [Ca(2+)](i) signals. Nutritional magnesium deficiency increases the susceptibility of the pancreas towards pathological stimuli. These data have prompted two clinical trials on the use of magnesium in patients at risk for pancreatitis.

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