

Subchronic oral intake of low cadmium doses affects intestinal immune responses in rats

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Gastrointestinal (GI) tract is one of the main targets of cadmium (Cd), important food and drinking water contaminant. In this study, the effect of subchronic (30 days) oral (in drinking water) intake of environmentally relevant doses of cadmium (5 µg/ml and 50 µg/ml) on intestinal [(tissue of duodenum and mesenteric lymph node (mLN) cells)] was examined in Dark Agouti (DA) rats. Atomic absorption spectrophotometry (AAS) analysis revealed significant cadmium load in duodenum, which was associated with changes of both intestinal bacterial load and composition (Denaturing Gradient Gel Electrophoresis/DGGE). Shortening of villi, damage to epithelium, increases in goblet-like vacuoles and mononuclear cell infiltration in lamina propria were histologically evident at both cadmium doses, with massive necrosis at higher Cd dose (judging by High Mobility Group Box-1/HMGB-1 Western blot analysis). Increased levels of proinflammatory cytokines (IL-1β, IFN-γ, IL-17) were observed at both Cd doses (TNFα at higher dose solely). Cadmium administration affected draining lymph nodes as well, judging by signs of stress response (drop of cellular reduced glutathione/GSH at higher dose, rise of metallothionein/MT mRNA at both doses). Increased cellularity of mLN was observed at higher Cd dose, but with no changes in proliferative responses. Intake of both Cd doses resulted in higher (compared to controls) levels of IFN-γ and IL-17 mRNA as well as increased mLN cell responsiveness to ConA stimulation. Significant increases in numbers of CD68+ cells and stimulation of innate immune activities (numbers of dihydrorhodamine/DHR+ cells and intracellular myeloperoxidase/MPO+ cells, LPS-stimulated nitric oxide/NO production and ex vivo IL-1β expression) were observed at higher dose of cadmium. Proinflammatory effects of cadmium might have resulted from changes in gut microbiota and tissue damage. Interactions of this metal with intestinal immune system should be taken into account when assessing dietary cadmium as health risk factor.

Funded by Ministry of Education, Science and Technological Development of Serbia (#173039).