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INFLUENCE OF CHRONIC INGESTION OF NITRATES AND NITRITES ON GASTROINTESTINAL NEUTROPHILS AND MAST CELLS IN RATS. P. Anton, V. Theodorou*, R. Garcia-Villar, P. Marche, L. Ressayre, J. Fioramonti, L. Buéno. INRA, Dept Pharmacology; *ESAP, Toulouse, France.

The presence of nitrates and nitrites in food and drinking water, as potential contaminants, nourishes an ongoing controversial human health issue. Potentially harmful effects of these compounds, or their by-products (nitrosamines, nitric oxide), have been linked to an alteration of the neuro-immune system which, physiologically ensures protection of the gastrointestinal mucosa. The present study, therefore, was undertaken to investigate the influence of a two-week oral administration of nitrate and nitrite salts to rats, at doses possibly found in food, on two major digestive immune cell types: mast cells and neutrophils.

Methods: Seven groups of 6 male Wistar rats (250-300 g) were used. Four groups received respectively: NaNO₃ (500 mg/kg/day), KNO₃ (250 mg/kg/day), NaNO₂ (8 mg/kg/day), or KNO₂ (5 mg/kg/day). Three groups served as controls and received respectively: distilled water (1 ml/day), KCl (183 mg/kg/day) or NaCl (341 mg/kg/day). After 14 days, rats were sacrificed and 2 cm segments of gastric antrum and jejunum (20 cm aboral to the ligament of Treitz) were collected for: (i) myeloperoxidase (MPO) spectrophotometric assay (an enzyme which characterizes neutrophil infiltration); and (ii) mast cell number determination (alcian blue/safranin staining and optic microscopy).

Results: The two parameters measured in both gastric antrum and jejunum were affected in variable proportions by the ingestion of the different salts in the four experimental groups (Table 1). In contrast, differences were not found in the control groups treated with KCl or NaCl compared to which received water.

Table 1: GI tissue responses to treatment in five groups (A: gastric antrum; J: jejunum; means±SEM; n=6).

	Tissue	Control	NaNO ₃	KNO ₃	NaNO ₂	KNO ₂
MPO (U/g prot.)	A	95±5	151±16*	59±12*	264±64*	938±194*
	J	92±32	14±3*	14±4*	95±20	159±50
Mast Cells (/mm ²)	A	76±6	97±20	38±12*	230±16*	106±37*
	J	114±13	114±19	122±26	155±24	114±19

* p<0.05; significantly different from the control group which received water; ANOVA and Bonferroni test.

Conclusion: Ingestion of nitrites for two weeks stimulates neutrophil infiltration and increases mast cell number in the gastric but not the intestinal mucosa suggesting a pro-inflammatory effect at the gastric level. Nitrates ingestion has opposite effects on neutrophil infiltration and mast cell number in the antrum depending on the type of salt used. In contrast, nitrites exert an anti-inflammatory effect at the intestinal level.

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