

GENDER-RELATED ROLE OF NITRIC OXIDE IN ELECTRICALLY EVOKED CONTRACTIONS IN HUMAN COLONIC CIRCULAR MUSCLE

Maselli M.A., Trisolini P., Pezzolla F., Demma I., De Ponti F.^o

Scientific Institute of Gastroenterology “S. de Bellis”, Castellana Grotte, Bari

^oDepartment of Pharmacology, University of Bologna, Bologna, Italy

Nitric oxide (NO) has been suggested as a possible mediator of the nonadrenergic, noncholinergic (NANC) relaxant response of many smooth muscle tissues and its role may vary with age. Little is known about possible gender-related differences. Therefore, we compared the effects of L-arginine methyl ester (L-NAME), an inhibitor of NO synthase, on electrically evoked contractions in colonic circular muscle from male and female patients. **METHODS.** Segments of sigmoid colon were obtained from 15 patients > 60 years, undergoing left hemicolectomy for non-obstructive sigmoid cancer. Patients were 10M (Group 1) and 5F (Group 2) (mean age 75yrs, range 66-82 yrs; mean age 77yrs, range 62-92 yrs; respectively). Colonic circular muscle strips were taken from macroscopically normal areas. Strips (15x3mm; deprived of the mucosa) were mounted isometrically in an organ bath with oxygenated Krebs solution at 37° C and placed under a tension of 20-24mN. After a 60 min stabilization period, at least two comparable response to carbachol (100µM) were recorded before studying the response to L-NAME. Strips were exposed to electrical field stimulation (EFS), evoked every 2 min delivering 10-s trains of pulses (0.1-10 Hz, duration 0.3 ms, 20V). The following drugs were tested: the association of atropine (2 µM) and guanethidine (5µM), the association of atropine, guanethidine, L-NAME (200µM), and tetrodotoxin (TTX, 2µM). Statistical analysis was performed by paired Wilcoxon test and Mann-Whitney U-test (difference between groups) as appropriate. P<0.05 was considered to be statistically significant. **RESULTS.** Electrically evoked contractions were linearly related to stimulation frequency and were significantly higher in Group 1 than Group 2 in the 3-10 Hz frequency range (p<0.05). Atropine and guanethidine inhibited electrically evoked contractions depending on stimulation frequency (p<0.01, p<0.05) in both groups. The further addition of L-NAME enhanced contractions, at all frequencies (p<0.01, p<0.05): this effect was significantly more pronounced in women. TTX abolished electrically evoked contractions both per se and after L-NAME indicating that they depend on action potentials generated in intrinsic nerves. **CONCLUSIONS.** We have shown a gender-related effect of L-NAME on electrically evoked contractions in human colonic circular muscle. Our results suggest a lower contribution of nitrenergic inhibitory pathways in men, in whom the higher magnitude of the electrically evoked contractions may be related to a less pronounced role of nitric oxide.