Detection of cytokine transcripts in rat gastric mucosa after exposure to stress using the reverse transcriptase polymerase chain reaction.

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Cytokines may contribute to the pathogenesis of stress ulcerations. They may be directly cytotoxic to epthelial cells, or may change the balance towards ulcer formation. Here we investigate the expression of several cytokine transcripts after a single exposure to stress.

Material and Methods: 25 rats were exposed to water restraint stress for 3.5h and then sacrificed at 0, 2, 4, 6 and 12h. The number of stress lesions were counted. Specimens were frozen in liquid nitrogen and total RNA was isolated. cDNA for RT-PCR was synthesized from RNA by reverse transcription using oligo(dT) priming. GAPDH, ß-actin, IL-1a, IL-2, IL-6,IFN-γ, TNF-α and TGFß1 transcripts were analysed by RT-PCR using specific primers.

Results: The average number of ulcerations at 0h was 15±3 and then gradually declined to 4 ± 2 at 12h after stress. Controls for ß-actin and GAPDH showed equal expression of transcripts, except that GAPDH transcripts were not detectable 2 h after stress induction. No IL-2, TNF-α, or IFN-γ transcripts were detectable. IL-6 was found in the control group and was also detectable 4 and 6 h after exposure to stress and decreased to below normal levels at 12h. A week signal for IL-1a was detectable at 4 h after exposure to stress. In contrast, TGFß1 transcripts decreased at 0 and 2 h after stress and its levels did not differ from those of controls at 4, 6, and 12 h after exposure to stress.

Conclusions: There is expression of a time-dependent pattern of cytokine gentranscripts after exposure to stress. This signaling of cytokines may reflect the normal biological response to stress.

INFLUENCE OF BLOOD MICROCIRCULATION ON THE ACUTE NSAID-INDUCED GASTRIC INJURY. J. Esteban*, M.A. Rodríguez*, J.R. Aracama*, C. del Pino*, M.J. Martín**, V. Motilva**, C. Alarcón**, D. Delgado**, J.M. Herrerías**. *Servicio Central de Investigación en Ciencias de la Salud de la Universidad de Cádiz. España. **Servicio de Aparato Digestivo. Hospital Virgen de Macarena. Universidad de Sevilla. España.

Mucosal blood microcirculation has been related with NSAID-induced gastric injury. Gastric mucosal blood microcirculation is controled by several mechanisms including nitric oxide (NO) and neuropeptide Y (NPY). In order to check the implication of both mechanisms in the injuring effect of the NSAID, we have investigated their effect on the mucosal levels of NPY and cGMP, as a measure of NO functionalism.

Wistar male rats (200-250 g body weigth) have been used.The NSAID administred have been: piroxicam 20, 10 and 5 mg/Kg; sodium diclofenac 100, 50, 25, 10, 5 and 2 mg/Kg, ibuprofen 100 and 50 mg/Kg and acetylsalicilic acid 500, 300 and 100 mg/Kg. A control group treated with saline solution has also been used. After a 24 h starved period the drug has been given and 3 h later the animals were anaesthetized (pentobarbital 20 mg/Kg i.p.), the stomachs were perfused with saline solution via abdominal aorta (15 ml/min), extracted and incised by minor curvature, the mucosal gastric injury was assessed using a standard scale and the mucosa was scraped and frozen at -70ºC until it is assessed. We have determined the mucosal NPY levels and cGMP concentration.The differences between NSAID treated groups and the saline group have been determined using the Kruskall-Wallis ANOVA followed by Mann-Whitney U-test when necessary.

The results obtained show that all NSAID used (except ibuprofen) induced a significative and dose-related decrease of cGMP concentration without modifying the mucosal NPY levels. For cGMP the results were: saline (2.88 pmol/mg protein), piroxicam (20 mg/Kg 0.78, 10 mg/Kg 0.68 and 5 mg/Kg 0.63 pmol/mg protein), diclofenac (100 mg/Kg 0.21, 50 mg/Kg 0.52, 25 mg/Kg 0.79 pmol/mg protein), acetylsalicilic acid (500 mg/Kg 0.87, 300 mg/Kg 0.86 pmol/mg protein).

These results are in agreement with the hypothesis that NSAID-induced gastric damage can be related with a decrease of NO functionalism.

TOPICALLY APPLIED NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND HOSPITALISATION FOR UPPER GI BLEEDING AND PERFORATION: A RECORD-LINKAGE CASE-CONTROL STUDY.

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Recent case reports have suggested an association between upper GI bleeding and perforation (UGIBP) and topical non-steroidal anti-inflammatory drugs (NSAIDs). ***Aim*** To evaluate the relationship between topical NSAIDs and hospitalisation for UGIBP. ***Methods*** A case-control study was carried out using a purpose built record-linkage database containing all dispensed prescribing data and all hospitalisation data for the population of Tayside, Scotland. There were 1,103 cases of UGIBP between Jan 90 and Dec 92 in the study population of 319,465 people, resident since Jan 89. Up to six age and sex-matched community controls (n = 6,593) and two hospital controls (n = 2,184) (with any diagnosis at the same hospital within 3 months of the case) were randomly generated from the study population. Exposure to topical NSAIDs, oral NSAIDs and ulcer healing drugs (UHD) 45 days prior to the index date and at any time from Jan 89 was assessed and modelled using conditional logistic regression. Results are given as odds ratios (OR) with 95% confidence intervals. ***Results*** The unadjusted ORs for the two exposure variables (45 day and Ever) are shown in the Table. Associations were evident for all three classes of drugs.

		Topical NSAIDs	Oral NSAIDs	UHD
Comm	45 day	2.6 (1.6, 4.2)	2.8 (2.3, 3.4)	4.6 (3.9, 5.5)
controls	Ever	1.5 (1.2, 1.9)	1.5 (1.3, 1.8)	4.3 (3.7, 5.0)
Hosp	45 day	1.6 (0.9, 2.8)	2.0 (1.6, 2.5)	1.9 (1.6, 2.3)
controls	Ever	1.0 (0.8, 1.2)	1.0 (0.9, 1.2)	1.8 (1.5, 2.1)

However, in a conditional logistic regression analysis which adjusted for the confounding effects of all three classes of drug simultaneously, there were no associations for topical NSAIDs. ORs were 1.5 (0.8, 2.5) and 1.1 (0.6, 1.9) with community and hospital controls respectively. 45 day exposure to oral NSAIDs was associated with UGIBP, with ORs of 2.6 (2.1, 3.2) and 2.0 (1.6, 2.5). Ever exposure to UHD was also associated with UGIBP. ORs were 4.2 (3.6, 4.9) and 1.8 (1.5, 2.1). ***Conclusion*** The results for oral NSAIDs and UHDs are consistent with other epidemiological studies. Topical NSAIDs were not significantly associated with hospitalisation for UGIBP after adjustment for confounding effects of oral NSAIDs and UHD.

PREVALENCE OF ESOPHAGEAL DISEASE AFTER BARIATRIC SURGERY. S.C. Fabry, T.A. Knox, and P.N. Benotti, Depts. of Gastroenterology and Surgery, New England Medical Center (NEMC), Boston, MA

Background: 1.5 million Americans have clinically severe obesity defined as a body mass index (BMI) over 40 kg/m2. Surgical options for obesity have been used with increasing frequency and success. These procedures are reported to reduce the risk of esophageal reflux disease. We have, however, noted a high prevalence of esophageal pathology in patients who have had bariatric surgery who underwent endoscopy. **Methods:** We retrospectively evaluated the prevalence of esophageal disease in 33 patients with prior bariatric surgery who underwent endoscopy at NEMC between June 1992 and August 1994. We reviewed endoscopic reports, operative notes, and hospital and clinic charts for data on type and date of surgery, symptoms necessitating endoscopy, and endoscopic findings. **Results:** Seventeen patients had had a gastric bypass procedure (primarily a Roux-en-Y gastrojejunostomy) and 16 patients a gastric partitioning procedure (gastrogastrostomy or gastroplasty). The main indications for endoscopy were abdominal pain, failure to lose weight, and vomiting. The mean age was 42.4 years and the mean interval since surgery was 5.1 years. Sixteen (48%) patients had esophageal pathology with 11 (33%) cases of esophagitis, 4 (12%) cases of abnormal motility, and 2 (6%) cases of Barrett's epithelium. The presenting complaints of these patients were comparable to those of the entire group. Eight patients had undergone a gastric bypass and 9 patients a gastric partitioning procedure. Eight patients had non-esophageal pathology (anastomotic stricture, mesh extruding into the stoma, marginal ulcer) that may have contributed to the esophageal disease but 8 patients had no other pathology No patients were noted to have both abnormal esophageal motility and esophagitis. One patient had abnormal motility and Barrett's epithelium. **Conclusions:** Esophageal pathology was found in 16/33 (48%) patients undergoing endoscopy. Eight of the 16 patients had no other pathology that could influence the esophageal findings. We hypothesize that reduction in gastric size influences esophageal function and increases the incidence of esophageal disease.