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COMPARISON STUDY ON EXPRESSION OF RMUC2 AND RMUC3 IN RAT WITH ULCERATIVE COLITIS.

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Aim: Colon mucosa produces two different kinds of mucins: goblet cells produce MUC2 mucin and columnar cells MUC3. A considerable number of reports have addressed the relationships of mucins and ulcerative colitis (UC). However, the comparison of MUC2 and MUC3 simultaneously on UC has not been investigated. The aim of this study was to make clear the role of MUC2 and MUC3 on UC. We investigated the changes of those mucins in dextran sulfate sodium(DSS)-induced colitis. **Methods:** Male Wistar rats weighing about 200 g were used. Five ml of 5% DSS (molecular weight 5,000) were introduced into the colon 6 cm from the anus via a catheter once a day for one week. Colonic tissues were excised on first, third, fifth and seventh day after the beginning of the DSS treatment. The colon was cut longitudinally, and the contents were removed by washing with cold phosphate buffered saline. The specimen was fixed in 10% buffered formalin solution. Thin sections were made and stained with hematoxylin and eosin or immunostained with anti-serum against rMuc2 and rMuc3. **Results:** DSS induced typical UC-like symptoms. Three days' treatment caused diarrhea and one week's treatment induced bloody diarrhea. Histological examination showed that three days' treatment induced infiltration of inflammatory cells, five days' treatment caused degeneration of the colonic gland and seven days' treatment caused further degeneration of the gland with loss of goblet cells at the distal portion. rMuc2 could no longer be detected after the disappearance of the goblet cells. On the contrary, the production of rMuc3 in columnar cells was as well conserved as the controls in spite of the inflammation of colon mucosa. **Conclusion:** One of the histological characteristics of UC is the depletion of goblet cells, while on the other hand, diarrhea with an excess of mucin and blood is also a major symptom of this disease. In reconciling this contradiction, our results suggest that the mucous stool of this disease results from rMuc3 mucin.

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THE HERBAL MEDICINE SHAKUYAKU-KANZOH-TOH RELAX GASTRIC SMOOTH MUSCLE AND INHIBIT ELECTRIC FIELD STIMULATION INDUCED ILEAL CONTRACTION VIA CHOLINERGIC PATHWAY.

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Background and aims: The herbal medicine, Shakuyaku-kanzoh-to (TJ-68) is a mixture of two popular herbs, shakuyaku (paeoniae radix) and kanzoh (glycyrrhizae radix) and has been experientially used for symptoms such as convulsion, spasm or abdominal pain for years. The clinical efficacy of TJ-68 is partly similar to scopolamine butylbromide (SB) which has adverse effects such as cardiac arrhythmia or glaucoma. TJ-68 has no these adverse effects. The mechanisms of action for TJ-68 to inhibit GI smooth muscle are not well known. Therefore, we undertook the study to elucidate the mechanisms of action of TJ-68 compared with SB on guinea pig gastric and ileal smooth muscle. **Methods:** The muscle strips of guinea pig gastric or ileal muscle was suspended from isometric transducers and TJ-68 was applied from lower concentration. All drugs were dissolved in water. The muscle strips were washed each time. Two components of TJ-68 were applied separately as same fashion. Electric field stimulation (EFS) (40V, 10Hz, 0.5ms) was applied with and without TJ-68 or its components. **Results:** TJ-68 (1mg/ml-10mg/ml) relaxed gastric muscle dose dependently. The relaxation was blocked by pretreatment with 10-5M of TTX. One of the components kanzoh (1mg/ml-10mg/ml) mimicked the relaxation while shakuyaku had no effect. SB did not cause gastric muscle relaxation. EFS stimulated ileal contraction was 78% blocked by TJ-68. Both components of TJ-68 blocked EFS induced contraction, however the mixture of two components (TJ-68) caused more prominent inhibition. Pretreatment with 10-5M of SB or 10-5M of atropine almost completely inhibited EFS induced contraction. **Conclusions:** TJ-68 had inhibitory effects on gastric and ileal smooth muscle. Action of TJ-68 on ileal muscle was considered to be the inhibition through cholinergic pathway which was similar to SB. Mixture of two herbs had additive effects compared with the each single component. This study was partly supported by Tsumura Co.Ltd.

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THE EFFECT OF H.PYLORI INFECTION IN REFLUX ESOPHAGITIS AND BARRETT'S ESOPHAGUS.

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We have reported that patients with reflux esophagitis(RE) have lower prevalence of H.pylori(HP) infection and milder gastric hyosecretion due to atrophic gastritis than the sex-age matched control subjects in Japan(AJG in press, Gastroenterol 1999;A217). Barrett's esophagus(BE) is thought to be an acquired condition resulting from severe gastroesophageal reflux. Recently GERD with BE increases gradually along with the decline of the prevalence of HP infection, although few studies have investigated the relationship between BE and HP infection. The aim of this study was to investigate the prevalence of HP infection, acid secretion and the grade of atrophic gastritis in RE patients with and without BE in Japan. **Materials and Methods:** A total of 114 patients with endoscopically diagnosed RE(male / female=63/51; age 61.2±13.3) were enrolled in this study. Long Segment BE(LSBE) and Short Segment BE(SSBE) was defined endoscopically as the presence of a columnar-appearing mucosa lining the distal esophagus extending proximally ≥3cm, and <3cm from the gastroesophageal junction, respectively. The prevalence of HP infection was determined by histology, rapid urease testing and the serum of IgG antibody. Gastric atrophy was evaluated by Pepsinogen (PG) I/II ratio. Gastric acid secretion was assessed by Endoscopic Gastrin Test(EGT), which we reported previously as a convenient method for the estimation of gastric acid secretion(AJG 1998;93:2113-8). **Results:** Of 114 RE patients, 35(30.7%) and 5(4.4%) were found to have SSBE and LSBE, respectively. The prevalence of BE tended to increase with age. Moreover, the severity of RE was significantly correlated with the length of a columnar-appearing mucosa (P<0.001). The prevalence of HP infection was lower in the BE patients than the RE patients without BE. (RE only;31.0%, SSBE;20.0%, LSBE;0%). PG/I ratio was higher in BE patients than RE patients without BE(RE only;4.56±1.66, SSBE;5.17±1.69, LSBE;5.08±0.79). EGT value(mEq/10min) was the highest in LSBE patients, but there was not significant difference among the three groups. (RE only;3.34±2.28, SSBE;3.56±1.67, LSBE;4.18±3.00). **Conclusion:** Our data showed that BE patients had the lower prevalence of HP infection, milder atrophic gastritis and higher acid secretion than patients without BE. In addition, the extension of columnar-appearing mucosa was associated with the severity of RE and aging. We suggest that HP may play a protective role against development of BE as well as RE in Japan.

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BARRETT'S ESOPHAGUS WITH SEVERE DYSPLASIA OR EARLY CANCER: RESULTS OF ENDOSCOPIC MUCOSEC-TOMY IN 17 PATIENTS.

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Introduction: The role of endoscopic mucosal resection (EMR) as curative therapy of severe dysplasia (SD) and early cancer in esophagus and stomach is well documented in the literature. In contrast, there is little data concerning the results of this treatment for severe dysplasia (SD) and early cancer in Barrett's esophagus. **Methods:** All consecutive patients with histologically proven Barrett's esophagus and SD or early cancer were prospectively included into the study. Using a standard monofilament polypectomy snare, EMR was performed after exclusion of deeper invasion by EUS (20 MHz miniprobe). **Results:** Between 11/94 and 10/99, 42 pts (9f/33m, median age 64 (47-88) yrs) with SD or early cancer of the esophagus or stomach underwent EMR. In 17 pts (4f/13m, median age 61(47-88) yrs) the lesions (median size 1 (0.4-2.5) cm) were associated with Barrett's esophagus. Histologically, 2 pts had SD and 15 early cancer (1 Ca in situ, 8 pT1m, 6 pT1sm). EUS was correct in 10/11 cases without invasion of the submucosa (91%) but only in 4/6 pts with submucosal invasion (67%). Snare resection was performed in all cases, supplemented in 4 cases by Argon plasma coagulation. Complications were bleeding during resection (5 pts, endoscopic hemostasis) and mild stenosis following multiple resections and repeated Argon plasma coagulation (1 pt, bougienage). There was no perforation and no procedure-related mortality. Two patients underwent surgical resection due to suspicion of incomplete removal of the tumor. In both cases the resected specimen were free of tumor. Two pts are currently being treated and one is lost to follow-up. Of the remaining patients, follow-up is 4 (1-33) months. Three pts died after 2,4 and 8 months, respectively (unrelated disease), the other patients are free of recurrence. **Conclusion:** Although the exact diagnosis of early submucosal invasion using EUS is not (yet) possible, diagnostic EMR after exclusion of deeper invasion is justified. Even in the presence of underlying Barrett's esophagus local resection may be curative in case of localized severe dysplasia or early cancer limited to the mucosa. These results have to be confirmed in long term studies.