FUNCTIONAL MAPPING OF PHASES OF SWALLOWING IN DORSAL VAGAL COMPLEX.

Ivan M. Lang, Caron Dean, Biduyut K. Medda, Reza Shakeri, Med Coll of Wisconsin, Milwaukee, WI.

Anatomical studies found that different subnuclei of the nucleus tractus solitarius (NTS) connect to pharynx and esophagus suggesting differential control during different phases of swallowing. Aim: To determine specific subnuclei of the dorsal vagal complex which control buccopharyngeal (BP) and esophageal (EP) phases of swallowing in a model with esophageal smooth and striated muscle. Methods: In 17 decerebrate cats, we recorded EMG from pharyngeal muscles to identify BP; and esophageal manometry to identify EP. BP and full (FS=BP+EP) swallows were activated by injection of water into pharynx. Activation of BP but not EP was done by transection of esophagus just below CP and bolus diversion. Transection alone did not prevent esophageal peristalsis during swallowing. Secondary peristalsis (SP) was activated by injection of air into midesophagus. Either FS (N=5), BP (N=4), or SP (N=4) were activated 0.5-3/mm for 3hrs. A sham procedure was used as control (Ctl, N=4). At end of experiment the brain was fixed, removed, and sections (40um) processed for c-fos immuno-reactivity or stained for thionin. c-fos nuclei were identified and counted using image processing software. Multiple comparison tests were used to determine significance (P<0.05). Results: We found the number of BP and EP events during Ctl, BP, SP and FS were respectively: 19±15 and 3±2, 249±34 and 2±1, 3±2 and 150±13, 271±54 and 135±15. Table lists mean±SE number of NTS and DMN c-fos nuclei at obex (com at 1.5mm caudal). BP expressed more fos in nL than SP, but SP expressed more fos in DMN, cen, and mn than BP. SP expressed more fos in DMN and mn than FS. BP and FS activated more dorsal regions of DMN than SP. The nL & vn did not respond significantly to any stimulus. Conclusions: 1) nL is associated with buccopharyngeal phase, 2) DMN and cen are associated with esophageal peristalsis, 3) nL and com may function in both phases, and 4) DMN may have an esophageal integrative function. These studies corroborate and provide evidence for some physiological conclusions of prior anatomical studies in the rat.

Tab: Intensity of symptoms, duration and frequency of consultation in the preceding 12 months for patients with and without psychiatric comorbidity.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Duration</th>
<th>Frequency</th>
<th>Consultation</th>
</tr>
</thead>
<tbody>
<tr>
<td>No psychiatric</td>
<td>30%</td>
<td>15%</td>
<td>77.8%</td>
</tr>
<tr>
<td>Psychic DSM</td>
<td>79.3%</td>
<td>60.4%</td>
<td>69.6%</td>
</tr>
<tr>
<td>DSM DX</td>
<td>&lt;0.02</td>
<td>Psychiatric DSM diagnosis vs. lifetime psychiatric diagnosis.</td>
<td></td>
</tr>
</tbody>
</table>

ATTENDING IBS CLASS REDUCES UTILIZATION OF SOURCES.

Michael J. Lawson, Roger Johnson, Tashia L. Orr, Mary P. Pauly, Kwesi Nigssah, Kaiser Permanente, Sacramento, CA.

Irritable Bowel Syndrome (IBS) accounts for at least 40% of gastroenterology practice. The syndrome leads to significant expenditure through sub-specialist consultation, emergency room visits and endoscopic evaluation. Patient education and behavioral modification are effective treatments in the management of IBS. We measured costs of caring for patients before and after a 2 hour IBS educational class consisting of physiological explanation by a gastroenterologist and behavioral change strategies by a clinical psychologist. Seventy-five IBS patients referred by the primary care providers were studied 18 months before and 18 months after the class for sub-specialist GI consultation, emergency room visits, primary care follow-up, psychiatric evaluation and endoscopic procedures. Seven patients (9%) had a GI consultation prior to the class. In the 18 months following the class only 4 of the 75 patients (5%) had a sub-specialty consultation with a potential cost savings of $3,638. Emergency room visits decreased 62%, primary care 13% and psychiatric evaluation 38%, with total savings in clinical visits alone of $28,106. Five percent of patients had lower GI endoscopy prior to the class. After the class only 12% of patients had lower GI endoscopy. (5 patients had flexible sigmoidoscopy and 4 had colonoscopy), resulting in further cost reductions. One patient was diagnosed with colon cancer. Resource utilization by IBS patients may be markedly reduced by education in a one-time group class setting, therefore allowing the condition to be managed by primary care.

TEGASEROD DOES NOT SIGNIFICANTLY AFFECT THE PHARMACOKINETICS AND PHARMACODYNAMICS OF WARFARIN IN HEALTHY SUBJECTS.

Matthias Langkauf, Gerald Holtmann, Lydia Buenger, Jutta Neufang, Univ Hosp, Suwon, South Korea.

Background: Tegaserod (HTF 919) is a 5-HT4 receptor partial agonist that is being developed for the treatment of irritable bowel syndrome. Objective: This open-label, randomized, 2-period crossover study evaluated the effects of multiple doses of tegaserod (TEG) on the pharmacokinetics (PK) and pharmacodynamics of warfarin (WAR) in healthy subjects. Plasma concentrations of R- and S-WAR were analyzed and prothrombin times (PT) were monitored up to 168 hours post-WAR dosing. Methods: After a 21-day screening period, 12 subjects between the ages of 20 and 41 were sequentially assigned a subject number corresponding to 1 of 2 treatment sequences. Subjects randomized to sequence 1 received WAR only in period I and WAR + TEG in period II. Subjects randomized to sequence II received WAR + TEG in period I and WAR only in period II. Each sequence had a baseline period, 2 treatment periods, and end-of-study evaluation. All subjects received 30 mg of WAR on day 4 of each treatment period. Subjects were given 6 mg of TEG twice daily on days 1 through 7 during the coadministration period. There was a 21-day interdose interval between WAR dosing in each treatment period. Results: Coadministration of TEG did not substantially alter the PK profile of R- or S-WAR. The AUC(0.00-24h) and Cmax for R- and S-WAR were similar with and without TEG. All subjects experienced PT elevations that were anticipated and consistent with the known onset of WAR anticoagulation. No significant differences were found between WAR and WAR + TEG with respect to average or maximum PT over 0 to 24h. Most of the close. More than 5 patients had a GI consultation in period I and WAR alone or in combination with WAR were well tolerated. Conclusion: The data suggest that dose adjustment is not needed when TEG is coadministered with WAR.

GLOBUS SENSATION IN KOREAN IS COMMONLY ASSOCIATED WITH ESOPHAGEAL DYSMOTILITY BUT NOT WITH GASTROESOPHAGEAL REFLUX.

Kwang-Jae Lee, Jin-Hong Kim, Ki-Baik Hahn, Sung-Won Cho, Ajou Univ Hosp, Suwon, South Korea.

Background: Globus sensation (globus) is best described as a constant feeling of a lump or fullness in the throat. In addition to emotional stress, mood, and personality disorders, globus has been associated with a hypertensive upper esophageal sphincter (UES), gastroesophageal reflux (GER),