Altered temporal characteristics of the rectoanal inhibitory reflex in patients with abdominal distension

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Shim L, Hansen RD, Prott GM, Morris LAI, Malcolm A, Kellow JE. Altered temporal characteristics of the rectoanal inhibitory reflex in patients with abdominal distension. Am J Physiol Gastrointest Liver Physiol 302: G1343–G1346, 2012. First published March 29, 2012; doi:10.1152/ajpgi.00400.2011.—The rectoanal inhibitory reflex (RAIR) is important in gas and stool evacuation. We examined RAIR features in patients with chronic constipation who exhibited bloating with and without abdominal distension, to determine whether alterations in RAIR may be a factor in the pathogenesis of abdominal distension. Seventy-five female patients with chronic constipation with or without abdominal distension were included in the study. The presence or absence of abdominal distension was assessed according to the Rome II questionnaire. All patients underwent both RAIR and rectal sensitivity testing, and specific RAIR parameters were analyzed. Patients were divided into two groups: abdominal bloating with distension (D, n = 55) and abdominal bloating without distension (ND, n = 20). D had a longer time to the onset of anal sphincter inhibition (latency of inhibition) (P = 0.03) compared with ND. In logistic regression analysis, a combination of age, latency of inhibition and the time measured from onset of inhibition to the point of maximum inhibition predicted abdominal distension (P = 0.002). There were no differences between groups for the time from point of maximum inhibition to recovery and for the percentage of internal anal sphincter relaxation. This is the first study to examine the role of RAIR in patients with abdominal distension. Female patients with constipation and abdominal distension exhibited differences in the temporal characteristics of, but not in the degree of, anal sphincter relaxation compared with patients without distension. Since this study was uncontrolled, further studies are necessary to determine the contribution of altered anorectal reflexes to abdominal distension.

constipation; bloating; rectal gas; anorectal function

THE RECTOANAL INHIBITORY REFLEX (RAIR), namely the transient relaxation of the internal anal sphincter in response to rectal distension, is considered to be important in discriminating rectal contents and in the maintenance of continence (7). In clinical practice, the RAIR is mainly designated as present or absent, for the diagnosis of Hirschsprung’s disease (19). However, like other enterorectonic reflexes (18, 20), the RAIR can be described in more detail by its individual components (11, 21, 30, 31). Thus Loening-Baucke et al. (16) showed that the degree of inhibition associated with the RAIR was significantly less in constipated children compared with healthy subjects. Xu et al. (30) also reported that patients with chronic constipation have an impaired percentage of anal sphincter relaxation induced by rectal distension compared with controls.

Patients with chronic constipation often complain of bloating, which may or may not be accompanied by abdominal distension (5). Proposed mechanisms for such abdominal distension include abnormal intestinal gas handling (22), rectal hyposensitivity (2), delayed intestinal transit (3), and abdominal hypochondric incoordination (1, 29). Recently, we have shown the importance of anorectal dysfunction in bloating and abdominal distension (23). In this latter study (23), prolonged rectal balloon expulsion time predicted the presence of abdominal distension in patients with constipation, suggesting that ineffective evacuation of gas and stool may be an additional mechanism for distension.

Because the RAIR may play an important role in efficient gas evacuation (4), we hypothesized that patients with chronic constipation and abdominal distension may exhibit differences in the RAIR, compared with patients without abdominal distension. Therefore, our aim was to quantify and compare the RAIR in a group of female patients with chronic constipation with and without abdominal distension.

MATERIALS AND METHODS

Patients. All female patients with chronic constipation and abdominal bloating referred to the Gastrointestinal Investigation Unit of Royal North Shore Hospital were considered for participation in the study. Patients completed both the Knowles Constipation Questionnaire (13) and the Rome Integrative Questionnaire (27). For entry to the study, patients were required to report abdominal bloating with a score of 1 or more (range 0–4) (13). Abdominal distension was assessed with the question “In the last year, have you seen your belly or abdomen swell up?” and considered present if reported more than 25% of the time (27). These patients also completed the Hospital Anxiety and Depression (32) questionnaire and a standardized obstetric/gynecological interview was undertaken. Patients were also required to fulfill symptom criteria for either functional constipation or non-diarrhoea irritable bowel syndrome (IBS) (27). Seventy-five female patients (means ± SD age 46 ± 16 yr) were included in the study. The protocol was approved by the Human Research Ethics Committee of the Royal North Shore Hospital and all patients gave informed consent.

RAIR and rectal sensitivity testing. Each individual study included evaluation of the resting anal sphincter pressure, the RAIR, and the rectal sensitivity to distension. Assessments were performed with patients lying in the left lateral position. To elicit the RAIR, a balloon attached to the end of an anorectal catheter was rapidly inflated with 50 ml air via syringe over 10 s in standardized fashion (19). Specifically, we used a 7-lumen water-perfused manometry catheter with 0.5-cm-spaced sideholes and a compliant silicone balloon (Dentsleeve International). The balloon measured 5.8 cm in length and 4.5 cm in width, and the intraballoon pressure measured in vitro at 50 ml inflation volume was 70 mmHg. The catheter was connected to calibrated pressure transducers, and data from the pressure transducers was displayed in digital form on a computer using data conversion software (Neomedix, Sydney, Australia). The onset of balloon inflation was recorded on the tracing. For rectal sensitivity testing, the same balloon was inflated with 100 ml air via syringe over 60 s in standardized fashion (26). The volume of air required to produce
RESULTS

Clinical features. Patients were subdivided into two groups according to the presence of abdominal distension: abdominal bloating with distension (D; n = 55; means ± SD age 44 ± 15 yr) and abdominal bloating without distension (ND; n = 20; age 52 ± 16 yr). D were significantly younger than ND (P = 0.04). There was no significant difference in the prevalence of patients with functional constipation and non-diarrhea IBS in those with distension (functional constipation 45%, non-diarrhea IBS 55%) vs. those without distension (functional constipation 45%, non-diarrhea IBS 55%). There was also no difference in the following parameters between the two groups (data not shown): scores for duration of symptoms, stool frequency and consistency, strain, blockage, incomplete emptying, anal pain, anxiety, and depression. There was also no difference in the mean parity (D 1.4 ± 0.2 vs. ND 1.9 ± 0.5) and in the number of patients with hysterectomy (D 24% vs. ND 35%) between the groups.

RAIR and rectal sensitivity. In all patients, the RAIR was present. There was no difference between groups in the first rectal sensation (D 66 ± 5 vs. ND 69 ± 10 ml, P = 0.8), urge to defecate (D 134 ± 9 vs. ND 135 ± 12 ml, P = 0.95), or maximum tolerated volume (D 207 ± 8 vs. ND 212 ± 15 ml, P = 0.8).

Resting anal sphincter pressure was higher in D (59 ± 3 mmHg) than in ND (50 ± 3 mmHg, P = 0.02). After adjustment for age and resting anal sphincter pressure, results for the parameters of RAIR are shown in Table 1. The Li was significantly longer in D vs. ND, and there was a nonsignificant trend for the Tmax to be longer in D vs. ND. There was also a trend for the inhibition slope to be lower in D vs. ND. There was no difference between groups for Trec,

### Table 1. Parameters of the RAIR in 75 female patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>D</th>
<th>ND</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latency of inhibition, s</td>
<td>6.5 ± 0.3</td>
<td>5.4 ± 0.3</td>
<td>0.03</td>
</tr>
<tr>
<td>Time measured from onset of inhibition to the point of maximum inhibition, s</td>
<td>5.9 ± 0.3</td>
<td>4.8 ± 0.5</td>
<td>0.07</td>
</tr>
<tr>
<td>Time from point of maximum inhibition to recovery, s</td>
<td>4.4 ± 0.3</td>
<td>4.7 ± 0.5</td>
<td>0.61</td>
</tr>
<tr>
<td>Inhibition slope, mmHg/s</td>
<td>5.8 ± 0.4</td>
<td>7.6 ± 1</td>
<td>0.06</td>
</tr>
<tr>
<td>Percentage of anal sphincter relaxation</td>
<td>53 ± 2</td>
<td>57 ± 5</td>
<td>0.48</td>
</tr>
<tr>
<td>Residual anal sphincter pressure, mmHg</td>
<td>26 ± 2</td>
<td>24 ± 3</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Data are expressed as means ± SE, with mean values adjusted for age and resting anal sphincter pressure. D, abdominal bloating with distension; ND, abdominal bloating without distension.

DISCUSSION

This is the first study to specifically examine the role of RAIR in patients with abdominal distension and chronic constipation. We have shown that differences in the RAIR were present in patients with abdominal distension, compared with patients without distension. Specifically, the Li was significantly longer in patients with distension, whereas the Tmax
A pattern of diurnal variation has been reported in patients with episodes of flatus evacuation is reduced. This reduced time gas in particular, the time available for passage of gas during that, in patients who experience distension related to intestinal during the RAIR could be more important in the normally
anal sphincter relaxation in our two groups of patients. Perhaps neurotransmitters associated with the intramural pathway.

Therefore, it is plausible that in our patients with abdominal distension.

RAIR is controlled by a neural reflex localized in the gut wall, independent of spinal cord involvement (8). Absence of the RAIR in patients with Hirschsprung’s disease strongly supports the concept of an intramural pathway for this reflex (15). Lubowski et al. (17) validated the intrinsic nature of the reflex by showing absence of the RAIR in subjects after circumferential myotomy of rectal circular smooth muscle. These investigators also demonstrated that the reflex is present after bilateral hypogastric nerve blockade and after complete isolation of the rectum from its extrinsic nerve supply, confirming that the RAIR is a local reflex within the wall of the anorectum (17). The RAIR is known to be mediated by endogenous nitric oxide, a neurotransmitter involved in the noradrenergic noncholinergic inhibitory nerves of the internal anal sphincter (24, 28). Using neuronal tracing techniques with enzyme histochemistry in an experimental guinea pig model, Stebbing et al. (24) showed that a nitrergic rectoanal neuronal pathway is responsible for mediating the RAIR. Recently, in animal mouse modeling, there was evidence that the nitrergic innervation is dependent on the presence of an intact network of interstitial cells of Cajal in the internal anal sphincter (6). Therefore, it is plausible that in our patients with abdominal distension there may be an alteration of the neurons and/or its neurotransmitters associated with the intramural pathway.

We were unable to demonstrate differences in the degree of anal sphincter relaxation in our two groups of patients. Perhaps the temporal characteristics of the RAIR could be more important in the normally relatively frequent passage of rectal gas, whereas the degree of relaxation of the anal sphincter during the RAIR could be more important in the normally relatively infrequent passage of stool. Therefore it is feasible that, in patients who experience distension related to intestinal gas in particular, the time available for passage of gas during episodes of flatus evacuation is reduced. This reduced time availability, on the order of up to 25%, could over the course of a day result in gradual intestinal gas accumulation. Indeed, a pattern of diurnal variation has been reported in patients with distension (5), in which the degree of distension is most prominent at the end of the day. We acknowledge, however, that this hypothesis is speculative, especially given the small differences in the RAIR parameters we detected. This finding of a subtle difference in the temporal characteristics of the RAIR could also have implications for future treatment. It is of interest that mosapride, a 5-HT4 agonist, has been shown in an experimental guinea pig model to enhance the RAIR, via actions on enteric neural 5-HT4 receptors (10, 14).

The technique of eliciting the RAIR has varied considerably in some reports. Most investigators have used a relatively rapid balloon inflation (11, 31). For example, Rao et al. (19) measured the presence or absence of RAIR in adults by rapidly distending the rectal balloon with 50 ml air, and this is the technique we employed in the present study. Loening-Baucke et al. (16), in contrast, elicited the RAIR in chronically constipated children by inflating the rectal balloon with different volumes of air (ranging from 5 to 60 ml). Our technique of a relatively rapid distension with 50 ml of air, although likely unphysiological, is a standard technique to elicit the RAIR and was chosen to maximize the unmasking of differences of the reflex parameters. Our finding of subtle differences in the altered temporal characteristics, specifically in patients with abdominal distension, is supported by two previous studies (11, 21) that have examined the RAIR parameters in patients and healthy subjects. Using 60 ml rectal balloon distension, Sangwan et al. (21) reported a mean latency of inhibition of 5.1 s in 14 healthy subjects. Importantly, this value of latency of inhibition, obtained by the same technique as in our present study, is virtually identical (5.4 s) to our finding with patients without abdominal distension, our disease control group. We believe, therefore, that it is reasonable to suggest that our group of patients with abdominal distension featured a longer latency of inhibition compared with healthy subjects reported in the literature. We acknowledge that we did not study a control group of healthy subjects and that this limits the conclusions we can draw.

Adjusting for age, which is a potentially important confounding factor, strengthens our results. Older patients may have a lower resting anal sphincter pressure due to decreased internal anal sphincter muscle tone (9). Therefore it is conceivable that increasing age may result in a lesser degree of anal sphincter relaxation during rectal distension. Another possible confounding effect is sex. Sun and Read (25) showed that a higher rectal volume is required to elicit an anal sphincter relaxation in men compared with women. We, therefore, performed our studies in women only, and consequently our findings are applicable to this sex only.

In conclusion, we have demonstrated that, in a group of 75 female patients with chronic constipation, those with abdominal distension exhibited differences in the temporal characteristics of the RAIR compared with those without distension. This suggests a potential role of the RAIR in the development of abdominal distension, perhaps by affecting the pattern of gas evacuation. Further studies will be required utilizing different distending volumes in a controlled study, and to explore in detail the nature and pattern of gas evacuation in patients with distension, for example, by objectively measuring rectal gas expulsion.
DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

L.S., A.M. and J.E.K. designed the study; G.M.P. and L.A.I.M. performed procedures; R.D.H. performed statistical analysis; L.S. wrote the paper and analyzed the data; A.M. and J.E.K. analyzed data, revised, and approved final version of paper.

REFERENCES