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A PHARMACOLOGICAL CHALLENGE PREDICTS REVERSIBLE RECTAL SENSORIMOTOR DYSFUNCTIONS IN WOMEN WITH FECAL INCONTINENCE

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Abstract

Background—In order to understand the pathophysiology of rectal sensorimotor dysfunctions in women with fecal incontinence (FI) and rectal urgency, we evaluated the effects of a muscarinic antagonist and an adrenergic α_2 agonist on these parameters.

Methods—First, rectal distensibility and sensation were evaluated with a barostat and sinusoidal oscillation at baseline and after randomization to intravenous saline or atropine in 16 healthy controls and 44 FI patients. Thereafter, FI patients were randomized to placebo or clonidine for 4 weeks; rectal compliance and sensation were reevaluated thereafter. The effect of atropine and clonidine on rectal functions and the relationship between them was evaluated.

Results—At baseline, compared to controls, rectal capacity was lower ($P=0.03$) while the mean pressure ($P=0.02$) and elastance ($P=0.01$) during sinusoidal oscillation were greater, signifying reduced distensibility, in FI. Compared to placebo, atropine increased ($P=0.02$) the heart rate in controls and FI and reduced ($P=0.03$) the variability in rectal pressures during sinusoidal oscillation in controls. Clonidine increased rectal compliance ($P=0.04$) and reduced rectal capacity ($P=0.03$) in FI. The effects of atropine and clonidine on compliance ($r=0.44$, $P=0.003$), capacity ($r=0.34$, $P=0.02$), pressures during sinusoidal oscillation ($r=0.3$, $P=0.057$), pressure ($r=0.6$, $p<0.0001$) and volume sensory thresholds ($r=0.48$, $P=0.003$) were correlated.

Conclusions—The effects of atropine and clonidine on rectal distensibility and sensation were significantly correlated. A preserved response to atropine suggests that reduced rectal distensibility is partly reversible, mediated by cholinergic mechanisms, and may predict the response to clonidine, providing a pharmacological challenge.

Graphical Abstract

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STATEMENT OF INTERESTS

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Women with urge FI have reduced rectal distensibility and increased sensation. Overall, atropine and clonidine had minimal effects on rectal capacity and compliance. However, the effects of atropine and clonidine on rectal distensibility and sensation were significantly correlated.

Keywords

Atropine; clonidine; fecal incontinence; rectal compliance; rectal capacity; urgency

BACKGROUND

A subset of women with FI have reduced rectal compliance or capacity and increased rectal sensation, which are associated with the symptom of rectal urgency. (1–4) Rectal urgency is associated with impaired quality of life.(5) Small series suggest that surgical augmentation of the rectum may benefit some patients.(6, 7) Restoring rectal distensibility with pharmacological modulation is another potential option. The α_2 -adrenergic agonist clonidine inhibits gastrointestinal motor activity by presynaptically inhibiting acetylcholine release from nerves in the myenteric plexus and at the neuromuscular junction.(8) Through these effects, and independently, via anti-nociceptive effects mediated by α_2 receptors in the spinal cord, brain stem, and forebrain, clonidine can also reduce sensation of distention.(9) Indeed, clonidine reduced colonic and rectal tone, increased colonic and rectal compliance, and reduced colonic and rectal perception of distention in healthy subjects (10, 11) and also improved symptoms in patients with diarrhea-predominant IBS.(12) In an uncontrolled study, clonidine improved symptoms in women with FI; this improvement was associated with increased rectal compliance and reduced rectal sensitivity.(13) However, in a subsequent, controlled, study, clonidine's effects on rectal distensibility and sensation and the relationship between changes in rectal sensorimotor dysfunctions and bowel symptoms were not significant.(14)

Nonetheless, the observations from the uncontrolled study suggest perhaps that rectal dysfunctions (i.e., a smaller rectal reservoir and increased rectal sensitivity) may be reversible in a subset of FI patients, who may perhaps be more likely to respond to treatment with an oral drug (e.g., clonidine) that modulates rectal compliance and sensation. Hence, the hypotheses of this study were: (i) Cholinergically-mediated mechanisms at least partly mediate reduced rectal distensibility and increased rectal sensation in women with urge FI and (ii) The effects of atropine and clonidine on rectal distensibility and sensation are correlated.

MATERIAL & METHODS

Study Design

After approval by the Mayo Clinic Institutional Review Board, this study was conducted at Mayo Clinic, Rochester MN. The study comprised 2 parts: an acute assessment, which was conducted in healthy controls and FI patients, and a short term trial comparing placebo and clonidine in FI patients only. During the acute study, rectal compliance and sensation were evaluated at baseline and after double-blind, randomization [1:1] to saline or atropine on the same day (Figure 1). During the short term trial, rectal compliance and sensation were evaluated before and 4 weeks after balanced, randomized [1:1], double-blind, placebo-controlled, treatment, parallel-group study with oral clonidine (0.1 mg twice daily). Treatment with clonidine was stratified by age (i.e., < 50 years and ≥ 50 years) and BMI (i.e., < 30 and ≥ 30 kg/m²).

The results of clonidine on bowel symptoms and rectoanal functions in FI patients have been reported.(15) However, the effects of atropine on rectal compliance and sensation in healthy controls and FI patients and the comparison of effects of atropine and clonidine have not been published. All personnel involved in the design and implementation of each trial remained unaware of the treatment assignments until the database was locked.

Eligibility Criteria

Women aged 18–75 years were eligible to participate. Healthy controls (age 34 ± 3 y, BMI 25 ± 0.8 kg/m²) were well and did not have symptoms of a functional bowel disorder by questionnaire. The patients (age 57 ± 2 y, BMI 29 ± 0.8 kg/m²) had urge-predominant FI as defined by a validated questionnaire for ≥ 1 year duration. As detailed previously, exclusion criteria for FI patients included current or prior organic colonic or anorectal diseases, severe diarrhea during the run in phase, clinically significant cardiovascular or pulmonary disease or EKG abnormalities, symptomatic hypotension, or systolic blood pressure of <100 mm Hg at initial screening visit, neurological disorders, use of opiate analgesics, and pregnancy or nursing.(15)

Assessment of Rectal Compliance and Sensation with a Barostat

Before the study, 2 sodium phosphate enemas (Fleets®, C.B. Fleet, Lynchburg, VA) were administered. Using validated techniques, rectal compliance and sensation were assessed with a barostat in the left lateral position with an “infinitely” compliant 7-cm long balloon with a maximum volume of 500 ml (Hefty Baggies, Mobil Chemical Co., Pittsford, NY) linked to an electronic rigid piston barostat (Mayo Clinic, Rochester, MN).(1, 2, 16) After a conditioning distention, rectal staircase distention (from 0 to 44 mm Hg or to maximum tolerated pressure, whichever came first, in 4-mm Hg steps at 1 minute intervals) was performed. Because atropine and clonidine may affect compliance, sensory thresholds were assessed with pressure-based rather than volume-based (ie, isobaric) distentions.(17) Using the volume during the last 30 seconds at each pressure, rectal pressure-volume relationships were analyzed with a power exponential function and summarized by the pressure corresponding to half maximum volume (P_{half}) and rectal capacity (i.e., maximum volume). (1, 18) Because some patients did not tolerate distention greater than 32 mmHg, only

pressures and volumes up to 32 mmHg were used to analyze these pressure-volume relationships, in order to standardize the analysis across participants. Rectal compliance and sensory thresholds for first sensation, desire to defecate, and urgency were recorded during the staircase distention; the threshold was the first sensation of each symptom.

Assessment of Rectal Distensibility with Sinusoidal Oscillation

Using validated techniques, rectal distensibility was also assessed with sinusoidal oscillation.(16, 19) After distending the balloon to 125 ml, it was oscillated at 5 counts/min for 20 min. Because the Institutional Review Board required that rectal pressures not exceed 48 mmHg during sinusoidal oscillation, the initial distending volume was reduced to 75 ml in 10 participants, all FI patients. As detailed previously,(19) balloon pressure, pump pressure, and pump volume were acquired at 10 Hz and analyzed with customized Lab-View based software. The balloon volume was calculated by using the actual pump pressure, actual pump volume and a correction factor determined from the in vitro studies. The pressure-volume loops were characterized for each cycle. Thereafter, the pressure waveform was separated into energy storage (i.e. elastic) and dissipative (i.e. resistive) components that were coupled to each other by hysteresivity (η), i.e., resistance $\approx \eta$ Elastance.(20) The formulae for calculating these parameters were detailed previously.(19) As the structural damping hypothesis suggests that resistance is dependent on elastance and hysteresivity, only data for pressures, elastance, and hysteresivity are presented.

Drugs

Similar to previous studies, atropine was administered intravenously, as a bolus of 0.015 mg/kg,(21–23) followed by an infusion at the rate of 0.01 mg/kg/hr, decreasing to 0.003 mg/kg/hr after 30 minutes, to ensure stable plasma levels throughout the study. This dose relaxed the colon in healthy people.(23)

Statistical Analysis

Rectal functions were summarized as Pr_{half} and maximum volume during the staircase distention, pressures, elastance, and hysteresivity during sinusoidal oscillation, and pressure and volume sensory thresholds for first sensation, desire to defecate, and urgency. The pressure level values for sensory thresholds that were not perceived by a given subject were considered as ‘censored’ using an approach described previously.(2) For example, when the first sensation threshold was not perceived, the pressure level for this threshold sensation was recorded as the pressure value for the desire to defecate, or urgency thresholds, or the maximum pressure during the curve, whichever came earlier, but labeled as “censored” (in contrast to pressure levels in which the subject indicated the first sensation threshold was perceived, which implied the “event” occurred).

Differences between healthy women and FI patients at baseline were evaluated with logistic regression models or the Cochran-Mantel-Haenszel test adjusting for age.

Treatment effects were analyzed per intent-to-treat analysis, with separate analysis of covariance models for rectal Pr_{half} , maximum volume during the staircase distention, mean and natural log of the standard deviation for pressures, elastance and hysteresivity during

sinusoidal oscillation, post atropine and, in patients, post clonidine. These models were adjusted for age, BMI, status (i.e., control or FI), the corresponding baseline (pre drug) parameter, drug effects (i.e., atropine or clonidine), and a drug*status interaction term.

Pre- and post-drug sensory thresholds were compared using separate proportional hazard regression models for each threshold type using a strata option to account for the matching (before vs. during therapy pairs). These models estimated the “risk” (probability) for reporting a specific sensation threshold over increasing pressure steps, analogous to a survival analysis of the risk for an event (e.g. death) over time.

The associations between effects of atropine and clonidine were assessed with the Spearman correlation coefficient.

RESULTS

Demographic and Clinical Features

The healthy controls were younger ($P < 0.001$) than FI patients (Table 1). The BMI was lower ($P < 0.005$) in healthy controls than FI patients. All 16 healthy participants and 44 FI patients completed all study procedures. Among FI patients, thirty eight patients had bowel symptoms (i.e., diarrhea-predominant IBS ($n=18$), functional diarrhea (4), functional constipation or constipation-predominant IBS (9), or diarrhea and constipation (7). As detailed previously, the FICA incontinence symptom severity score suggested moderate (25 patients) or severe FI (19 patients).

Differences in anorectal parameters between health and FI at baseline

Table 1 demonstrates that before adjusting for age, rectal distensibility was lower in FI than in controls. Thus, the Pr_{half} was greater ($P=0.004$) while rectal capacity was lower ($P < 0.0001$) in FI while mean pressures ($P < 0.0001$) and mean elastance ($P=0.004$) during sinusoidal oscillation were greater in FI. The average rectal capacity in FI (189 ml) was 30% lower than in healthy controls (272 ml). Of note, the pressures during sinusoidal oscillation were greater in FI patients even though the starting volume was 75 ml in 10 of 44 FI patients, versus 125 ml in all controls. Likewise, volume, but not pressure, thresholds for the desire to defecate ($P=0.03$) and urgency ($P=0.02$) were lower in FI, suggesting increased sensitivity, in FI than in healthy women.

Even after adjusting for age, which was a significant covariate in all models, rectal capacity was lower ($P=0.03$) in FI, while the mean pressure ($P=0.02$) and elastance ($P=0.01$) during sinusoidal oscillation were greater, signifying reduced distensibility, in FI than in healthy controls. In addition, the variability in hysteresivity ($P=0.02$) was greater in controls than in FI. However, after adjusting for age, rectal compliance (Pr_{half}) and sensory thresholds were not significantly different between health and FI (Table 1).

Effects of atropine on heart rate

In healthy women, atropine increased heart rate (105 ± 8 per minute after versus 64 ± 3 per minute before) to a greater extent ($P=0.02$) than placebo (71 ± 6 per minute after versus 65 ± 3 per minute before). Likewise, in patients, the heart rate increased to a greater extent

($P<0.0001$) after atropine (88 ± 3 per minute after versus 68 ± 3 per minute before) than saline (68 ± 2 per minute after versus 65 ± 2 per minute before).

Effects of atropine on rectal compliance and capacity measured with a barostat

By comparison to saline, atropine did not increase the maximum rectal volume (rectal capacity) in healthy women or FI patients (Table 2). Likewise, atropine did not increase rectal compliance relative to placebo in healthy women or in FI.

Effects of atropine on rectal sensation and relationship with heart rate

Atropine did not affect the pressure and volume thresholds for first sensation, desire to defecate, or urgency in healthy women or FI patients (Table 3).

Among healthy women, pressure and volume thresholds for first sensation ($r=-0.29$, $P=0.27$ for pressure; $r=-0.15$, $P=0.59$ for volume), desire to defecate ($r=-0.23$, $P=0.39$ for pressure, $r=-0.13$, $P=0.62$ for volume) and urgency ($r=0.30$, $P=0.32$ for pressure, $r=0.22$, $P=0.47$ for volume) were not correlated with heart rate. Similarly, drug effects on rectal compliance ($r=0.07$, $P=0.80$) and rectal capacity ($r=-0.07$, $P=0.79$) were not correlated with heart rate. Similarly, among women with FI, the correlations between the effects of atropine on heart rate and compliance (i.e., Pr_{half} and maximum capacity) and sensory thresholds were also not significant (data not shown).

Effects of atropine on rectal distensibility during sinusoidal oscillation

Atropine did not significantly affect the mean pressure (Table 4). However, atropine reduced the variability in pressures, expressed as $\ln SD$, in healthy ($P=0.03$) and in FI patients ($P=0.04$); the interaction term (drug*status) was not significant ($P=0.93$) indicating similar effects in healthy participants and FI patients. Neither atropine nor clonidine altered rectal elastance or hysteresivity in healthy women or FI (data not shown).

Effects of clonidine on rectal compliance, capacity, and sensation

By comparison to placebo, the rectal Pr_{half} was greater ($P<0.05$) and the rectal capacity was lower ($P=0.03$), after clonidine in FI patients (Table 2). Clonidine did not affect the pressure and volume thresholds for first sensation, desire to defecate and urgency in FI (Table 3).

Relationships between effects of atropine and clonidine on rectal compliance and rectal sensation

The effects of atropine and clonidine on rectal compliance ($r=0.44$, $P=0.003$), rectal capacity ($r=0.34$, $P=0.02$) (Figure 2) and rectal stiffness during sinusoidal oscillation ($r=0.3$, $P=0.057$) were correlated. Pressure and volume thresholds for first sensation ($r=0.57$, $P=0.0002$ for pressure; $r=0.23$, $P=0.15$ for volume), desire to defecate (Figure 3) ($r=0.61$, $P<0.0001$ for pressure, $r=0.48$, $P=0.003$ for volume) and urgency ($r=0.45$, $P=0.006$ for pressure, $r=0.52$, $P=0.001$ for volume) were correlated.

Atropine's effects on rectal compliance (Pr_{half}) and capacity were not significantly correlated with its effects on sensory thresholds (first sensation, desire to defecate, and urgency).

DISCUSSION

Confirming previous studies from our group (1, 2, 16) and others,(3) women with urge FI had reduced rectal distensibility, manifesting as lower rectal capacity and greater rectal pressures during sinusoidal oscillation. To emphasize, on average, the rectal capacity during barostat distention was 30% lower while pressures during sinusoidal oscillation were twofold greater in FI than in controls. Volume thresholds for the desire to defecate and urgency were also lower in FI patients, likely reflecting reduced rectal distensibility. While women with FI were older than controls, most differences at baseline between healthy women and FI patients were significant even after adjusting for age. Moreover, increased age is associated with *reduced* rectal sensation and does not affect rectal capacity in asymptomatic women.(24)

The atropine dose used in this study reduced esophageal stiffness, gastric antral motor activity, colonic tone, and the contractile response to colonic distention.(22, 23, 25) In this study, atropine increased the heart rate but not rectal capacity or compliance, confirming a previous report (21) in which the same bolus dose of atropine but no infusion was given. Taken together, these findings suggest that in healthy humans, cholinergic tone under fasting conditions is more prominent in the colon than the rectum. It is conceivable that a higher dose of atropine may reduce rectal tone. In vervet monkeys, intravenous atropine (1 mg/kg), which is approximately 60× greater than the bolus dose used in our studies, inhibited rectal “peristaltic contractions”.(26) It is also possible that atropine may have a greater effect on rectal tone and compliance under postprandial conditions, when cholinergic tone is increased.

However, the effects of atropine on rectal sensorimotor functions varied among participants. Moreover, the effects of atropine and clonidine on rectal compliance, capacity, and sensation were correlated. This is consistent with the hypothesis that stimulation of adrenergic α_2 receptors by clonidine inhibits colonic tone by reducing acetylcholine release from neurons in the myenteric plexus and at the neuromuscular junction,(8) and suggests that the acute response to atropine provides a pharmacological challenge that may predict the long term effects of clonidine. Perhaps a preserved response to atropine suggests that increased rectal stiffness is, at least partly, due to excess cholinergic tone and reversible. We cannot explain why clonidine increased the $P_{r_{half}}$, suggesting reduced rectal compliance, and reduced rectal capacity in FI patients. These effects were small but statistically significant.

In many conditions (eg, ventricular arrhythmias), the acute pharmacological effects serves as a pharmacological challenge, guides, and predicts the response to long term therapy.(27) By comparison, the acute response to a drug (i.e., a pharmacological challenge) is infrequently used to guide the management of gastrointestinal motility disorders. Perhaps the most striking example is the use of the acute colonic contractile response to neostigmine or bisacodyl to diagnose colonic inertia and identify patients who require colectomy.(28) The acute effects of neostigmine on colonic transit and compliance predicted the effects of pyridostigmine on colonic transit in patients with autonomic neuropathy and constipation. (29)

Quasi-static pressure-volume relationships (i.e., compliance curves) evaluated with a barostat measure rectal capacity and compliance. During these staircase distentions, the active contractile (or dynamic) response is allowed to subside while pressure and volume equilibrate at each distending pressure.(23) Rectal pressure-volume relationships that are evaluated after a conditioning distention are reproducible among individuals.(30, 31) However, in this study, the rectal capacity was greater after than before saline. Whether this is due to altered rectal biomechanical properties or displacement of extra-rectal structures after the first distention is unknown.(32)

During sinusoidal oscillation, the colon or rectum are continuously distended, and for a longer time, thereby assessing the quasi-static and dynamic responses to distention. Similar to its effects on rectal compliance and capacity, atropine did not affect the mean pressure during sinusoidal oscillation. However, atropine did reduce the variability in rectal pressures during sinusoidal oscillation, which probably reflects the active contractile response to distention. This suggests that sinusoidal oscillation provides a more refined assessment of the active contractile response to distention than rectal pressure-volume relationships evaluated with a barostat.

In summary, this study confirms that a subset of FI patients have reduced rectal distensibility and increased rectal sensation, demonstrates that these sensorimotor dysfunctions are reversible in some patients, and underscores the need to develop additional options for managing reduced rectal distensibility in FI.

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Key Points

- Women with urge FI have reduced rectal distensibility and increased sensation.
- Overall, atropine and clonidine had minimal effects on rectal capacity and compliance.
- However, the effects of atropine and clonidine on rectal distensibility and sensation were significantly correlated,
- which suggests that atropine provides a pharmacological challenge to predict the effects of clonidine.

Figure 1. Experimental design

In controls and patients, rectal distensibility and sensation were evaluated before and after randomization to saline or atropine. In patients, rectal functions were reevaluated after they had been treated for placebo or clonidine for 4 weeks. During that second study, rectal distensibility and sensation were only evaluated once, after placebo or clonidine was administered on the day of the study.

Figure 2. Relationship between effects of atropine and clonidine on rectal capacity and rectal compliance

Observe the significant correlation between effects of atropine and clonidine on rectal compliance (left panel) and capacity (right panel).

Figure 3. Relationship between drug effects of atropine and clonidine on pressure (left panel) and volume (right panel) sensory thresholds for the desire to defecate

Figure 4. Pressure-volume relationship during rectal staircase distention (0–44mmHg) from a healthy woman before and after atropine

At 32 mmHg, the balloon volume was 275 ml before and 298 ml after atropine. The event marker depicts symptoms i.e., first sensation (1), desire to defecate (2), and urgency (3) recorded by the patient.

Figure 5. Balloon pressures and volumes during sinusoidal oscillation at 5 cpm before and after atropine, and, balloon volume in a healthy woman (panel A) and FI (panel B)
Balloon pressures were approximately twofold greater in the FI patient.

Table 1

Baseline anorectal parameters in healthy women and FI patients

Anorectal parameters	Healthy women (N=16)	FI patients (N=44)
Age	34 ± 3	57 ± 2 [‡]
BMI (kg/m ²)	25 ± 0.8	29 ± 0.8 [*]
Barostat assessments		
Rectal compliance, Pr _{half} (mmHg)	12.3 ± 0.7	16.1 ± 0.5 [‡]
Rectal capacity (ml)	272 ± 11	189 ± 7 [‡]
Sensory thresholds		
First sensation – Pressure (mmHg)	16.2 ± 2.8	16.4 ± 1.6
First sensation – Volume (ml)	140 ± 21	81 ± 9
Desire to defecate – Pressure (mmHg)	20 ± 2.3	20.4 ± 1.5
Desire to defecate – Volume (ml)	172 ± 20	110.3 ± 10 [*]
Urgency – Pressure (mmHg)	26.8 ± 2.5	21 ± 1.5
Urgency – Volume (ml)	230 ± 19	152 ± 10 [*]
Sinusoidal oscillation		
Mean pressure (mmHg)	9.1 ± 1.0	17.2 ± 0.9 [‡]
Mean elastance (mmHg/mL)	0.20 ± 0.03	0.30 ± 0.02 [‡]
Mean hysteresivity	−0.05 ± 0.21	0.19 ± 0.01
SD of pressure (mmHg)	2.9 ± 1.4	2.6 ± 0.2 [‡]
SD of elastance (mmHg/mL)	0.06 ± 0.01	0.09 ± 0.01 [‡]
SD of hysteresivity	0.10 ± 0.01	0.11 ± 0.01

All values are Mean ± SEM unless stated otherwise

^{*} p < 0.05,[‡] p = 0.01[‡] p = 0.001 by Wilcoxon rank sum test.

Table 2

Effects of Pharmacological Modulation on Rectal Capacity and Rectal Compliance

	Rectal compliance, Pr_{half} (mmHg)		Rectal capacity (ml)	
	Before	After	Before	After
Healthy women – placebo	12 ± 1	11 ± 1	262 ± 11	279 ± 10
Healthy women – atropine	13 ± 1	12 ± 1	284 ± 20	292 ± 16
Fecal incontinence – placebo	17 ± 1	15 ± 1	180 ± 10	205 ± 8
Fecal incontinence – atropine	15 ± 1	15 ± 1	199 ± 10	230 ± 9
Fecal incontinence – placebo	16 ± 1	16 ± 1	186 ± 11	206 ± 11
Fecal incontinence – clonidine	17 ± 1	18 ± 1 *	193 ± 10	185 ± 9 *

All values are Mean ± SEM,

*
p<0.05

Table 3

Effects of Pharmacological Modulation on Sensory Thresholds

	First Sensation				Desire to defecate				Urgency			
	Pressure		Volume		Pressure		Volume		Pressure		Volume	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Healthy women – placebo	18 ± 5	17 ± 4	142 ± 35	177 ± 26	19 ± 4	21 ± 3	151 ± 33	209 ± 23	23 ± 4	25 ± 3	196 ± 28	248 ± 19
Healthy women – atropine	14 ± 2	17 ± 3	137 ± 23	168 ± 17	21 ± 2	23 ± 3	199 ± 15	224 ± 21	31 ± 1	29 ± 2	270 ± 17	263 ± 13
Fecal incontinence – placebo	16 ± 3	20 ± 3	74 ± 14	125 ± 18	20 ± 2	25 ± 3	98 ± 14	153 ± 15	27 ± 2	31 ± 2	139 ± 13	185 ± 13
Fecal incontinence – atropine	16 ± 2	20 ± 2	90 ± 10	155 ± 13	21 ± 2	24 ± 3	126 ± 13	182 ± 15	27 ± 2	28 ± 3	168 ± 16	207 ± 14
Fecal incontinence – placebo	16 ± 2	16 ± 3	79 ± 14	92 ± 19	20 ± 2	21 ± 3	110 ± 16	126 ± 19	25 ± 2	28 ± 3	142 ± 17	167 ± 16
Fecal incontinence – clonidine	17 ± 2	19 ± 2	83 ± 12	81 ± 13	21 ± 2	22 ± 2	111 ± 12	104 ± 12	29 ± 2	30 ± 2	161 ± 12	156 ± 12

All values are Mean ± SEM. Pressure and volume are expressed as mmHg and ml respectively.

Effects of Pharmacological Modulation on Rectal Distensibility during Sinusoidal Oscillation

Table 4

	Mean Pressure (Mean $\pm$ SEM, mmHg)		SD of Mean Pressure (geometric mean [CI], mmHg) [†]	
	Before	After	Before	After
Healthy women – placebo	8 $\pm$ 1	9 $\pm$ 1	0.9 (0.6 – 1.5)	1 (0.6 – 1.8)
Healthy women – atropine	11 $\pm$ 2	11 $\pm$ 1	1.2 (0.8 – 1.9)	0.9 (0.6 – 1.3) *
Fecal incontinence – placebo	18 $\pm$ 1	16 $\pm$ 1	1.7 (1 – 2.7)	1.7 (1.1 – 2.7)
Fecal incontinence – atropine	17 $\pm$ 1	16 $\pm$ 1	1.8 (1.1 – 2.9)	1.3 (0.7 – 2.5) *
Fecal incontinence – placebo	16 $\pm$ 2	16 $\pm$ 1	1.7 (1.1 – 2.5)	1.7 (1.1 – 2.5)
Fecal incontinence – clonidine	18 $\pm$ 1	18 $\pm$ 1	1.7 (1 – 3)	2 (1.4 – 3)

* p<0.05 versus before atropine.

[†]The natural log of SD (lnSD) for mean pressure was analyzed. Summary estimates are expressed in original format as geometric mean values.