Supplementary Content

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1. Sensitivity analyses

Three sensitivity analyses (1 preplanned and 2 post hoc) were conducted for the outcomes. First, the preplanned analysis was based on the per-protocol analyses, in which the participants accepted the assigned treatment and finished the treatment protocol. Second, the change in the total IBS-SSS from baseline to week 6 was analyzed by fitting a mixed-effect model. Third, change from baseline in the total IBS-SSS and IBS-QOL total score was examined using multivariate regression model.

1.1 Analysis based on per-protocol analyses

To assess the robustness of the primary analysis, we also ran analysis based on per-protocol population. The results showed in per-protocol analyses were similar to our primary analysis. For the primary outcome, the mean change in the total IBS-SSS at week 6 was greater in the acupuncture group (135.12) than in the PEG 4000/pinaverium group (94.41) with a mean difference of 40.72 (95%CI, 23.88 to 57.55; $P< .001$).

Supplemental Table 1. Primary outcome and secondary outcomes based on per-protocol analyses.

Variable	Acupuncture group (n=314)	Polyethylene glycol 4000/ pinaverium bromide group (n=153)	Difference (95%CI)	P value [a]
Primary outcome				
Change of the total IBS-SSS at week 6, mean (95%CI)	135.12 (125.44, 144.80)	94.41 (80.63,108.18)	40.72 (23.88, 57.55)	< .001
Secondary outcomes				
Change, the total IBS-SSS, mean (95% CI)				
Week 1	45.18 (38.23, 52.14)	30.69 (21.96, 39.42)	14.49 (3.36, 25.62)	.01
Week 2	75.42 (67.53, 83.31)	54.42 (44.86, 63.99)	21.00 (8.63, 33.36)	<.001
Week 4	106.20 (97.57, 114.84)	75.71 (63.96, 87.46)	30.49 (15.68, 45.30)	<.001
Week 18	138.65 (128.89, 148.42)	88.45 (74.62, 102.28)	50.20 (33.25, 67.16)	<.001
Change, IBS-QOL total score, mean (95% CI)				
Week 6	14.43 (12.69,16.18)	9.99(7.60,12.38)	4.44(1.44, 7.44)	.004
Week 18	17.53(15.55,19.50)	10.41(7.80,13.02)	7.12(3.76, 10.47)	< .001
Post hoc analysis				
Responder rate, n(%) [b]				
Week 6	261 (83.12)	96 (62.75)	20.38 (11.67, 29.09%)	< .001
Week18	274 (87.26)	86 (56.21)	31.05 (22.37, 39.74%)	< .001

Abbreviations: IBS-SSS= IBS-symptom severity score; IBS-QOL= IBS quality of life; CI=confidence intervals.

a. All tests were 2-sided. *P* value of less than 0.05 was considered significant.

b. Patients with a reduction of 50 points or more on IBS-SSS total score were defined as responders.

1.2 Mixed-effect model results on reduction in the total IBS-SSS.

The change from baseline in the total IBS-SSS at weeks 6 and 18 were analyzed by fitting a mixed-effect model using baseline value as a covariate, treatment as a fixed effect, and site as random effects accounting for center differences. For the primary outcome, the mean change in the total IBS-SSS at week 6 was greater in the acupuncture group (80.36) than in the PEG 4000/pinaverium group (64.15) with a mean difference of 16.22 (95%CI, 7.29 to 25.14; $P< .001$).

Supplemental Table 2. Mixed-effect model results on reduction in the total IBS-SSS

Variable	Acupuncture group (n=344)	Polyethylene glycol 4000/ pinaverium bromide group(n=175)	Difference (95%CI)	P value [a]
Change of the total IBS-SSS from baseline, adjusted mean (95%CI)				
Week 6	80.36(69.95,90.78)	64.15(52.57,75.73)	16.22(7.29,25.14)	< .001
Week 18	120.39(102.50,138.28)	86.81(67.83,105.80)	33.58(22.36,44.79)	< .001

Abbreviations: IBS-SSS= IBS-symptom severity score; CI=confidence intervals

a.   All tests were 2-sided. *P* value of less than 0.05 was considered significant.

1.3 Multivariate Regression Model on reduction in the total IBS-SSS and IBS-QOL total score

The change from baseline in the total IBS-SSS was analyzed by a multivariate regression model using several baseline factors as covariates, including baseline the total IBS-SSS /IBS-QOL total score (when change in the total IBS-SSS from baseline was analyzed, baseline total IBS-SSS was set as a covariate; on another occasion, baseline total IBS-SSS was set as a covariate), site, age, sex, weight, treatment history of IBS, coexisting illness, duration, subtype of IBS and *5-HTTLRP* alleles. The results were similar to our primary analysis.

Supplemental Table 3. Multivariate Regression Model on change in the total IBS-SSS and IBS-QOL total score

Variable	Acupuncture group (n=344)	Polyethylene glycol 4000/ pinaverium bromide group(n=175)	Difference (95%CI)	*P* value [a]
Change in the total IBS-SSS from baseline, adjusted mean (95%CI)				
Week 6	134.91 (114.98,154.83)	102.97 (81.67,124.28)	31.93 (17.94,45.93)	< .001
Week 18	133.33 (109.00,157.66)	85.88 (59.87,111.89)	47.45 (30.36,64.54)	< .001
Change in the IBS-QOL total score from baseline, adjusted mean (95%CI)				
Week 6	14.55(10.69,18.41)	10.64(6.52,14.77)	3.90(1.21,6.60)	.005
Week 18	17.24(12.79,21.68)	10.43(5.67,15.18)	6.81(3.70,9.91)	< .001

Abbreviations: IBS-SSS= IBS-symptom severity score; CI=confidence intervals.

a. All tests were 2-sided. *P* value of less than 0.05 was considered significant.

2. IBS-SSS scores and five domains of IBS-SSS between baseline, 6-week treatment period and 12-week follow-up

Supplemental Table 4. Total IBS-SSS and five domains of IBS-SSS between baseline, 6-week treatment period and 12-week follow-up
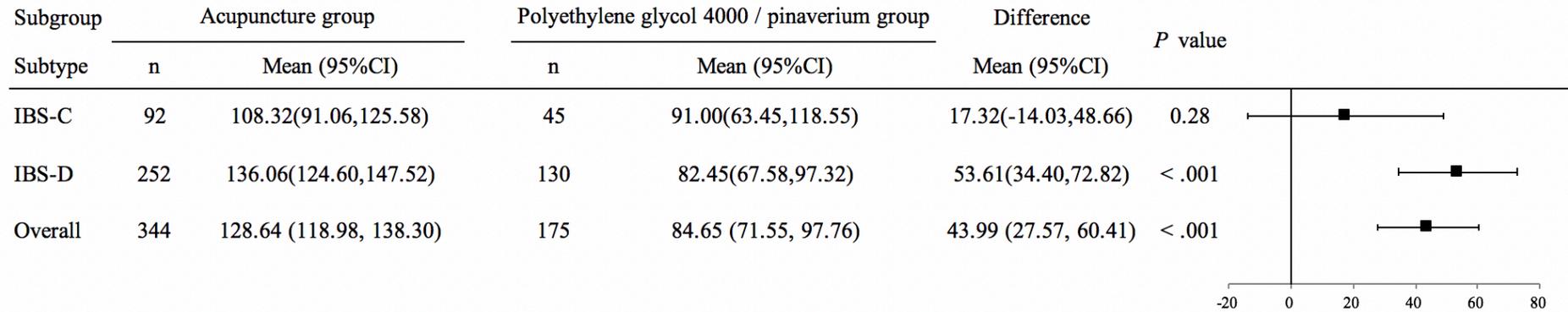
(mean±SD)

IBS-SSS	Baseline	Week 1	Week 2	Week 4	Week 6	Week 18
Total IBS-SSS						
Acupuncture group(n=344)	246.44±82.94	201.65±76.68	173.22±68.75	145.14±68.29	117.80±67.37	114.58±74.44
PEG 4000/pinaverium bromide group(n=175)	225.88±86.78	198.45±81.90	178.13±73.54	157.66±72.19	141.23±70.86	146.43±78.78
P value	.009	.66	.45	.05	< .001	< .001
Severity of abdominal pain						
Acupuncture group(n=344)	35.74±28.17	27.42±24.16	23.18±20.59	18.52±18.37	14.83±16.52	14.75±17.79
PEG 4000/pinaverium bromide group(n=175)	32.31±27.20	26.89±23.78	24.09±20.98	21.60±20.32	18.89±19.12	20.49±21.08
P value	.18	.80	.71	.14	.04	.004
Number of days in pain every 10 days						
Acupuncture group(n=344)	3.34±2.91	2.57±2.36	2.19±2.06	1.82±1.96	1.40±1.76	1.44±1.90
PEG 4000/pinaverium bromide group(n=175)	2.91±2.60	2.37±2.27	1.97±1.93	1.78±1.81	1.54±1.76	1.70±1.83
P value	.20	.40	.26	.93	.22	.02
Severity of abdominal distension						
Acupuncture group(n=344)	39.15±28.67	30.56±25.10	24.49±22.12	20.15±19.37	15.63±18.15	14.68±17.97
PEG 4000/pinaverium bromide group(n=175)	31.11±29.61	27.91±27.26	24.54±24.27	20.46±21.74	18.23±19.61	18.66±21.46

P value	.002	.19	.82	.75	.20	.11
Satisfaction with bowel habits						
Acupuncture group(n=344)	71.73±18.77	59.98±19.47	53.12±19.28	45.34±20.25	37.82±20.80	36.99±21.88
PEG 4000/pinaverium bromide group(n=175)	68.11±21.53	61.67±20.26	55.53±19.82	49.63±20.29	45.17±21.33	45.87±22.10
P value	.07	.54	.29	.02	< .001	< .001
Interference of IBS with life in general						
Acupuncture group(n=344)	66.38±19.48	58.02±19.76	50.51±19.91	42.96±20.15	35.58±20.40	33.79±20.46
PEG 4000/pinaverium bromide group(n=175)	65.25±21.17	58.32±21.67	54.31±19.89	48.20±20.19	43.57±20.22	44.42±21.41
P value	.47	.92	.05	0.005	< .001	< .001

Abbreviations: IBS-SSS= IBS-symptom severity score; SD=standard deviation; PEG 4000= Polyethylene glycol 4000.

3. Subgroup Analysis

Supplemental Figure 1. Forest plot of subgroup analysis according to IBS subtype on change in the total IBS-SSS at week 6.

Subgroup	Acupuncture group		Polyethylene glycol 4000 / pinaverium group		Difference	P value	
Subtype	n	Mean (95%CI)	n	Mean (95%CI)	Mean (95%CI)		
IBS-C	92	108.32(91.06,125.58)	45	91.00(63.45,118.55)	17.32(-14.03,48.66)	0.28	
IBS-D	252	136.06(124.60,147.52)	130	82.45(67.58,97.32)	53.61(34.40,72.82)	< .001	
Overall	344	128.64 (118.98, 138.30)	175	84.65 (71.55, 97.76)	43.99 (27.57, 60.41)	< .001	

Abbreviations: CI=confidence intervals; IBS= irritable bowel syndrome; IBS-C= constipation predominant IBS; IBS-D= diarrhea predominant IBS