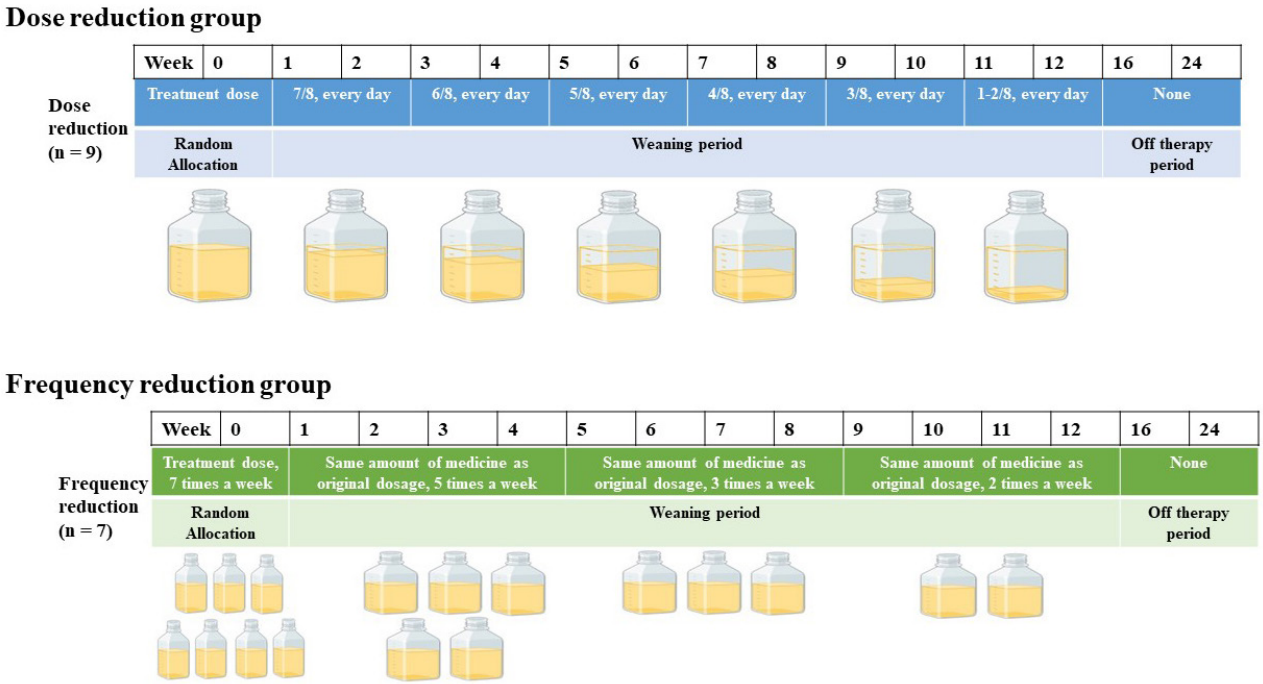

Figure S1 Study protocol. In the dose reduction group, the daily dosage of lactulose was reduced by approximately 1/8 of the initial dose every 2 weeks during the weaning period. In the frequency reduction group, the number of medication administrations per week was gradually reduced from 7 to 2 times every 4 weeks, while the daily dosage was maintained.

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Table S1 Comparisons of results by drug reduction methods

Variable	Weeks	Analysis method	Dose reduction (n=9)	Frequency reduction (n=7)	P
Dose of lactulose (ml/day)	Week 4	ITT	15 (10–26)	30 (10–50)	0.06
		PP	18 (7–26)	35 (20–50)	0.06
	Week 8	ITT	12 (10–22)	30 (10–50)	0.02
		PP	13 (4–22)	35 (20–50)	0.045
	Week 12	ITT	7.5 (0–18)	20 (0–50)	0.01
		PP	5.75 (3–18)	35 (20–50)	0.01
Dose of lactulose (ml/kg/day)	Week 4	ITT	1.17 (0.41–1.68)	1.48 (0.65–3)	0.14
		PP	1.29 (0–2)	1.79 (1–3)	0.12
	Week 8	ITT	0.93 (1–1)	1.77 (1–3)	0.08
		PP	0.93 (0–6)	1.77 (1–3)	0.39
	Week 12	ITT	0.45 (0–1)	1.53 (0–3)	0.006
		PP	0.41 (0–1)	1.74 (1–3)	0.01
Frequency of taking lactulose (per week)	Week 4	ITT	7 (7–7)	5 (5–5)	<0.001
		PP	7 (7–7)	5 (5–5)	<0.001
	Week 8	ITT	7 (0–7)	3 (3-3)	0.09
		PP	7 (7–7)	3 (3-3)	0.004
	Week 12	ITT	7 (0–7)	2 (1–2)	0.009
		PP	7 (7–7)	2 (1–2)	0.003

Data are presented as medians with ranges. ITT, intention-to-treat; PP, per-protocol; NA, non-applicable.

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Table S2 Overall clinical outcomes during the weaning period

Weeks	Clinical outcomes	Analysis	Dose reduction	Frequency reduction	Total	P
Week 4	Bowel movement ≥3 per week	ITT	7/9 (77.8%)	7/7 (100%)	14/16 (87.5%)	0.48
		PP	7/9 (77.8%)	7/7 (100%)	14/16 (87.5%)	0.48
	Bristol Stool Form Scale ≥3	ITT	9/9 (100%)	7/7 (100%)	16/16 (100%)	NA
		PP	9/9 (100%)	7/7 (100%)	16/16 (100%)	NA
	Absence of painful defecation	ITT	7/9 (77.8%)	4/7 (57.1%)	11/16 (68.7%)	0.60
		PP	7/9 (77.8%)	4/7 (57.1%)	11/16 (68.7%)	0.60
Week 8	Bowel movement ≥3 per week	ITT	9/9 (100%)	7/7 (100%)	16/16 (100%)	NA
		PP	6/6 (100%)	7/7 (100%)	13/13 (100%)	NA
	Bristol Stool Form Scale ≥3	ITT	9/9 (100%)	6/7 (85.7%)	15/16 (93.8%)	0.44
		PP	5/6 (83.3%)	6/7 (85.7%)	11/13 (84.6%)	>0.99
	Absence of painful defecation	ITT	7/9 (77.8%)	6/7 (85.7%)	13/16 (81.2%)	>0.99
		PP	4/6 (66.7%)	6/7 (85.7%)	10/13 (76.9%)	0.56
Week 12	Bowel movement ≥3 per week	ITT	8/9 (88.9%)	5/7 (71.4%)	13/16 (81.3%)	0.18
		PP	5/6 (83.3%)	4/4 (100%)	9/10 (90%)	>0.99
	Bristol Stool Form Scale ≥3	ITT	9/9 (100%)	5/7 (71.4%)	14/16 (87.5%)	0.18
		PP	6/6 (100%)	4/4 (100%)	10/10 (100%)	NA
	Absence of painful defecation	ITT	9/9 (100%)	7/7 (100%)	16/16 (100%)	NA
		PP	6/6 (100%)	4/4 (100%)	10/10 (100%)	NA

ITT, intention-to-treat; PP, per-protocol; NA, non-applicable.

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Table S3 Adverse events

Symptoms	Weeks	Analysis	Dose reduction (n=9)	Frequency reduction (n=7)	P
Abdominal pain	Week 4	ITT	2/9 (22.2%)	2/7 (28.6%)	>0.99
		PP	2/9 (22.2%)	2/7 (28.6%)	>0.99
	Week 8	ITT	0	2/7 (28.6%)	0.18
		PP	0	2/7 (28.6%)	0.46
	Week 12	ITT	1/9 (11.1%)	0	0.17
		PP	1/6 (16.7%)	0	>0.99
Vomiting	Week 4	ITT	0	0	NA
		PP	0	0	NA
	Week 8	ITT	0	0	NA
		PP	0	0	NA
	Week 12	ITT	0	0	NA
		PP	0	0	NA
Abdomen distension	Week 4	ITT	2/9 (22.2%)	0	0.48
		PP	2/9 (22.2%)	0	0.48
	Week 8	ITT	0	0	NA
		PP	0	0	NA
	Week 12	ITT	0	0	NA
		PP	0	0	NA
Diarrhea	Week 4	ITT	0	1/7 (14.3%)	0.44
		PP	0	1/7 (14.3%)	0.44
	Week 8	ITT	1/9 (11.1%)	0	0.36
		PP	0	0	NA
	Week 12	ITT	0	0	NA
		PP	0	0	NA

Data are presented as the numbers with percentages. ITT, intention-to-treat; PP, per-protocol; NA, non-applicable.

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