CHAPTER IV

RESULTS

Initial Patient Characteristics

A total of 99 patients, and their parents were asked to participate and enter the one week of run-in phase of our study. After the run-in phase, 5 patients were excluded because their parents declined to participate. Therefore, 94 patients were enrolled in the study.

The 47 patients were randomly allocated into the PEG group and 47 into the MOM group. Figure 3 summarizes the flow of participants through the run-in, enrollment and completion phase of the study protocol.

A total of 89 patients completed the study. Five patients did not complete the study, 1 in the PEG group due to illness (acute bronchitis) and 4 in the MOM group were lost to follow up.

Table 4 shows the baseline characteristics of the study patients. Patients in both groups were comparable in all demographic data and initial patient characteristics. The mean age of the patients was 2.58 years in both groups. Mean body weight was 12.85 and 13.2 kg. in the PEG and MOM group respectively (p=0.56). There were more males in the MOM group than PEG group (49% vs 33% respectively) but this was not statistically significant (p=0.12). Median stool frequency before treatment was 3 episodes per week in both groups (p=0.15). Median duration of constipations was 52 weeks in both PEG and MOM group (p= 0.63). Previous laxative treatment was 13% in the PEG group and 9.3% in the MOM group (p=0.74) with average duration of previous laxative treatment about 1 week in both groups (p=0.80). Family history of constipation was 63% and 53% in the PEG and MOM group respectively (p=0.36).

Median total Rome III criteria for enrolling the patients was 4 criteria in both groups. The distribution of each criteria are shown in table 5. All study patients had

history of painful on defecation as shown as Rome criteria IV of everyone in both groups. Table 6 shows initial physical examination of the study patients.

Figure 3: **Flow of participants through the run in phase, enrollment and completion of the study protocol (The CONSORT flow chart)**

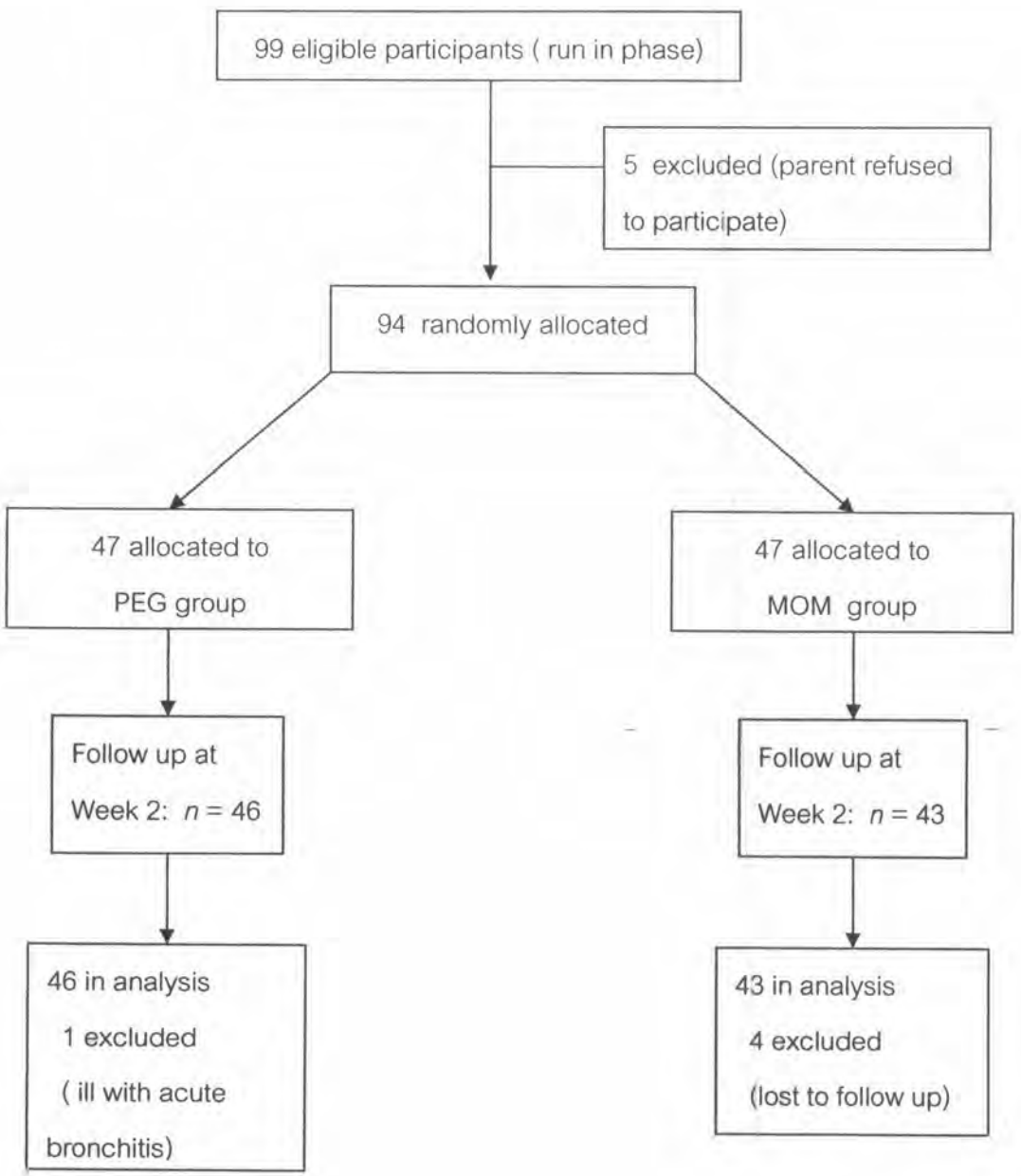

Table 4: Baseline characteristics of the participants by treatment group

Characteristics	PEG (N = 46)	MOM (N = 43)
	Mean(SD)	Mean(SD)
Age in years	2.58 (0.84)	2.58 (1.01)
Body weight in kilograms	12.85 (2.61)	13.20 (3.08)
	Median(Q_1, Q_3)	Median(Q_1, Q_3)
Stool frequency, episodes per week	3 (2, 4)	3 (2, 5)
Duration of constipation in weeks	52 (24, 69)	52 (20, 104)
	n(%)	n(%)
Sex, male	15 (33)	21 (49)
Previous treatment with laxatives	6 (13)	4 (9.3)
Family history of functional constipation	29(63)	23(53)

Table 5: Rome III criteria of the participants by treatment group

Criteria	PEG (N = 46)	MOM (N = 43)
	n(%)	n(%)
Criteria I: Stool frequency ≤ 2 episode/wk.	21(46)	20(47)
Criteria II: Fecal incontinence frequency ≥ 1 episode/wk.	1(2.2)	1(2.3)
Criteria III: History of excessive stool retention	45(98)	39(91)
Criteria IV: History of painful or hard bowel movement	46 (100)	43 (100)
Criteria V: Presence of abdominal and/or rectal fecal mass	36 (78)	29 (67)
Criteria VI: History of large-diameter stools that may obstruct the toilet	26 (57)	27 (63)
	Median(Q_1, Q_3)	Median(Q_1, Q_3)
Total number of Rome III criteria met	4(3,5)	4(3,4)

Table 6: Initial physical examination of the participants by treatment group

Physical examination	PEG (N = 46)	MOM (N = 43)
	n(%)	n(%)
Normal	16(35)	19(47)
Abnormal		
Distend abdomen	1(2.2)	1(2.3)
Fecal mass	2(4.3)	3(7.0)
Anal fissure	17(37)	7(16)
Perianal skin tag	6(13)	6(14)
Anal fissure and perianal skin tag	4(8.7)	6(14)

Primary outcome analyses

Forty two patients (42/46) in the PEG group and twenty eight patients (28/43) in the MOM group exhibited improvement after 4 weeks of treatment. Compared with the patients in the MOM group, the patients in the PEG group had significantly higher improvement (improvement rate 91% vs 65 %, p = 0.003). Moreover, after 2 weeks of treatment when the patients came for follow-up at the middle point of the study, the improvement in the PEG groups were also significantly higher than in the MOM groups (63% vs 42%, p =0.045).

When looking at the patients without improvement, 2 patients in PEG group still had stool frequency less than 3 episodes/week and 2 other patients still had painful defecation with bleeding from anal fissure. In the MOM group, 4 patients still had stool frequency less than 3 episodes/week and 11 patients still had painful defecation after 4 weeks of treatment.

The treatment effect as primary outcome, showed the difference in proportion of patients with improvement between the 2 groups after 4 weeks of treatment. It was 26 % (95% CI 9.8%, 43%). The calculated number needed to treat was 4.

As a sensitivity analysis, those who were lost to follow up at the end of the study were included in a further analysis of primary outcome, assuming that these individuals did not improve. The patients in the PEG group still had more improvement than patients in the MOM group after 4 weeks of treatment (89% vs 60%, p=0.001).

Dietary fiber intake during treatment in both groups was recorded on daily dietary charts by parents. All data were analyzed using information from the Table of Nutritive values of Thai food, Division of Nutrition, Ministry of Public Health (36) and by consultation with a nutritionist. As for duration of constipation, duration of previous laxative treatment before treatment and the family history of functional constipation, the amount of daily dietary fiber intake during treatment in both groups were not significantly different (2.70 vs 2.64 gm/ day, p =0.82).

Secondary outcome analyses

1. Improvement in stool frequency

The initial frequency of bowel movements per week was higher than expected in both groups. However, every study patients met two or more Rome III criteria for diagnosis of functional constipation. Therefore, there was no need to have a stool frequency $\leq$ 2 episodes/week as criteria I in every case.

The stool frequency at initial, 4 week follow up visit and the difference in improvement in stool frequency are shown in Table 7. Compared with patients in the MOM group, the patients in the PEG group had more improvement in stool frequency after 4 weeks of treatment (p = 0.04).

In this study, there were only 2 patients with fecal incontinence (1 in PEG, another in MOM group). Because the age of patients in this study was $\leq$ 4 years, we expected a low incidence (about 2%) in our patients. However, both patients exhibited

improvement, as fecal incontinence frequency became less than 1 episode/ week after 4 week of treatment.

Table 7: Improvement in stool frequency between PEG and MOM

Stool frequency (episodes/wk.)	PEG (N = 46)	MOM (N = 43)	Mann Whitney test	
	Median(Q_1, Q_3)	Median(Q_1, Q_3)	Z	P
Initial visit	3(2,4)	3(2,5)	-1.44	0.15
4 wk. follow-up visit	6(4.75, 7)	5(4,7)	-0.79	0.43
Improvement[a]	3(1,4)	2(0,3)	-2.07	0.04

[a] Improvement in stool frequency = Stool frequency: after – before medication

2. Adverse effects

During the 4 week study period, no serious adverse events were recorded in either group. Overall adverse effects in both groups were not significantly different (p=0.245). The symptoms of adverse effects as observed were abdominal pain/discomfort, bloating/ flatulence and nausea/ vomiting. All were mild and transient. However, patients in the MOM group had more diarrhea than those in the PEG group (28% vs 4.3%, p=0.002), but the diarheal episodes were resolved after reducing the dosages. No patient was withdrawn from the study due to adverse effects.

3. Compliance rate

The patients in the PEG group had a better compliance rate than patients in the MOM group (89% vs 72%, p=0.041). Parents of patients who received MOM recorded that their children did not like the taste of MOM, even if it was mixed with juice. The patients who were counted as non-compliance in this study received <80% of the medication. No any patient in either group continued to refuse medications because all of the patients were still young and their parents continued to give medications. .

Table 8 shows the adverse events and the compliance rate recorded by parents.

Table 8: Adverse effects and compliance rate by treatment group

Variable	PEG (N = 46)	MOM (N = 43)	χ_1^2	P
	n(%)	n(%)		
Any adverse effect	20(44)	24(56)	1.353	0.245
Diarrhea	2(4.3)	12(28)	9.306	0.002
Abdominal pain/ discomfort	9(20)	14(33)	1.958	0.162
Bloating/ flatulence	13(28)	13(30)	0.042	0.838
Nausea/ vomiting	4(8.7)	(21)	2.667	0.102
Compliance rate$^{\varepsilon}$	41(89)	31(72)	4.175	0.041

$^{\varepsilon}$Compliance rate: defined as the proportion of patients who received $\geq$ 80% of the medication throughout the study

Treatment doses

The median PEG treatment dose at the 4-week follow up evaluation was 0.5 g / kg body weight daily (Q_1, Q_3 0.4, 0.6). The median PEG doses were similar for patients who had and had not experienced improvement (p=0.75).

The median MOM treatment dose at the 4-week follow up evaluation was 0.6 ml /kg body weight daily (Q_1, Q_3 0.5, 0.7). The median MOM doses were also similar for patients who had and had not experienced improvement (p=0.88).

We also found that the patients in the PEG group had significantly more weight gain than those in the MOM group (0.63 vs 0.18 kg., p= 006) at 4 week follow-up.