

Effectiveness of amitriptyline for treating functional dyspepsia in adolescents

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Abstract

Background Functional dyspepsia is common among adolescents. Pain reduces children's quality of life, psychosocial functioning, and school attendance. Amitriptyline is assumed to be one of the alternative treatments in functional dyspepsia.

Objective To investigate the effectiveness of amitriptyline as a treatment for functional dyspepsia in adolescents.

Methods We conducted a randomized, single-blind, controlled trial from January to March 2011 in junior and senior high school students in Dobo City, Aru Island District, Maluku Province. Adolescents suffering from functional dyspepsia and who fulfilled the inclusion criteria were eligible for the study. Subjects were randomized into two groups. Each group received 10 mg (for body weight < 35 kg) or 20 mg (for body weight ≥ 35 kg) amitriptyline or placebo once per day for 28 days. Pain frequency was measured in terms of abdominal pain episodes per month, and duration was measured in minutes. Data were analyzed using t-test.

Results Eighty-eight students participated in this study: the amitriptyline group (43 subjects) and the placebo group (45 subjects). There were no statistically significant differences between the amitriptyline and placebo groups in frequency ($P=0.777$; 95%CI -0.846 to 1.129) or duration ($P=0.728$) of abdominal pain after treatment.

Conclusion Amitriptyline is not more effective than placebo for treating functional dyspepsia in adolescents. [Paediatr Indones. 2016;56:262-6 doi: 10.14238/pi56.5.2016.262-6].

Keywords: amitriptyline; functional dyspepsia; adolescent

Dyspepsia is the most common cause for medical consultations in children.¹ The symptoms of dyspepsia are common, occurring in 26-34% of the general population in the United States.² Pain reduces children's quality of life, psychosocial functioning, and school attendance.³

Functional dyspepsia is considered to be self-limiting and reported to be associated with anxiety disorders and depression. It may also be accompanied by headache and complaints in other parts of the body, necessitating treatment or health services. Sleep disorders, as well as significantly increased school absences are also consequences of functional dyspepsia.^{3,4}

In children, pharmacologic treatment of functional dyspepsia has been mostly empirical and based on adult data. There have been a few small,

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randomized, clinical trials evaluating the efficacy of drugs for the treatment of functional dyspepsia in children.^{5,6} One pharmacological therapy that can be given is an anti-depressant, such as amitriptyline.⁷ A small dose of amitriptyline has been suggested as an alternative therapy for functional dyspepsia.¹

The aim of our study was to investigate the effectiveness of amitriptyline as a treatment for functional dyspepsia in adolescents.

Methods

We conducted a single-blind, randomized, controlled trial from January to March 2011 at three junior/senior high schools in Dobo City, Aru Islands, Maluku. We included adolescents aged 12 to 18 years diagnosed with functional dyspepsia according to the ROME III criteria,⁸ who experienced episodes at least once per week for at least two months prior to diagnosis. Subjects had persistent or recurrent pain or discomfort centered in the upper abdomen (above the umbilicus), not relieved by defecation nor associated with the onset of a change in stool frequency or stool form, and with no evidence of inflammatory, anatomic, metabolic or neoplastic processes that explained the subjects' symptoms.^{9,10} We excluded those who refused

to take medication, those with weight loss, failure to thrive, vomiting, chronic diarrhea, fever of unknown origin, abnormal stool, organ enlargement, or pain due to menstruation.

Before starting the study, we explained the study methods, effects and treatment of functional dyspepsia to the subjects and their parents. On presentation, a standard history was taken, a thorough physical examination was performed by a physician and parents were asked to fill questionnaires.

Subjects were randomized by a random table method into two groups. The treatment group received amitriptyline doses of either 10 mg, for those with body weight <35 kg, or 20 mg, for those with body weight \geq 35 kg, once daily. The placebo group received placebo once daily. The subjects were advised to take the medicine at night for 28 days. For blinding purposes, the amitriptyline and placebo were formulated in capsules of the same color. We were aware of the amitriptyline or placebo given to subjects. Each group recorded the frequency and duration of functional dyspepsia symptoms in a daily diary given for 2 months. If the abdominal pain still persisted, subjects were allowed to take paracetamol (500 mg every 8 hours). The study was approved by the Ethics Committee of the University of Sumatera Utara Medical School.

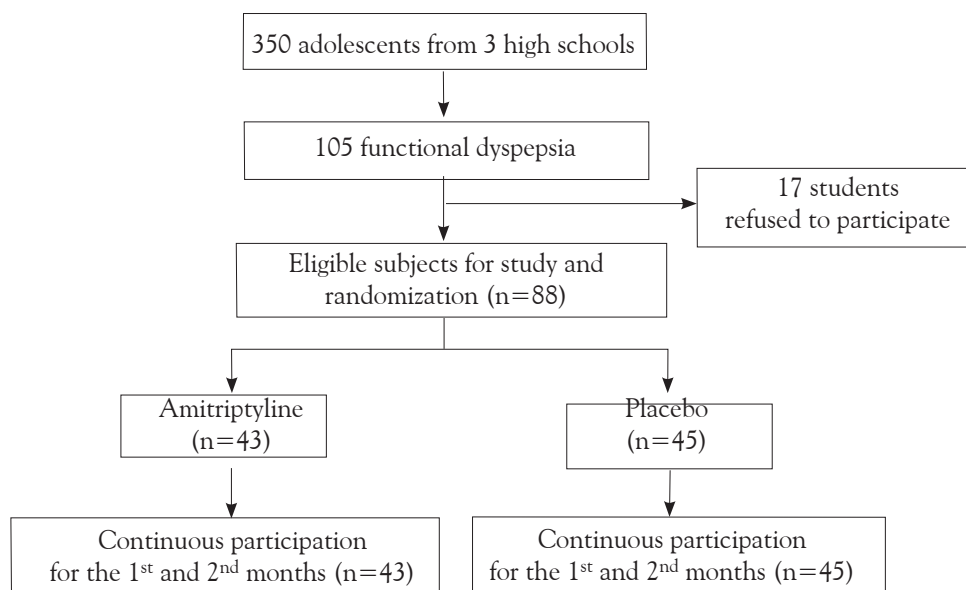


Figure 1. Study flow chart

Seventeen students refused to participate in the study, so the remaining 88 children were included in the study and randomized into two groups, the amitriptyline (43 subjects) and placebo (45 subjects) groups. After two months of follow-up, no subjects dropped out. The prevalence of functional dyspepsia in adolescents aged 12 to 18 years was 27.6% (Figure 1).

Table 1 shows the baseline characteristics of each group before intervention. The majority of adolescents with functional dyspepsia were female. Table 2 shows the comparison of amitriptyline to placebo with regards to frequency and mean duration of dyspepsia after 4 weeks of treatment. There was a significant difference in frequency of dyspepsia after 1 month of treatment ($P = 0.007$; 95%CI: 0.385 to 2.404), but no significant difference at 2 months after the start of treatment ($P=0.777$; 95%CI: -0.84 to 1.129). There were no significant differences in duration between the two groups after 1 month ($P=0.941$) and 2 months after the start of treatment ($P=0.728$).

Table 1. Baseline characteristics of subjects

Characteristics	Amitriptyline (n=43)	Placebo (n=45)
Gender, n(%)		
Male	11 (25.6)	8 (17.8)
Female	32 (74.4)	37 (82.2)
Mean age (SD), years	14.7 (1.24)	14.9 (1.36)
Mean weight (SD), kg	41.3 (5.28)	42.5 (6.08)
Mean height (SD), cm	148.7 (6.77)	150.9 (5.40)
Mean frequency of dyspepsia (SD), episodes per mo	8.7 (3.55)	6.0 (2.04)
Median duration of dyspepsia, n(%)		
< 10 min	18 (41.9)	15 (33.3)
10-30 min	22 (51.20)	14 (51.1)
30-60 min	3 (7)	6 (13.3)
>60 min	0	1 (2.2)

Table 2. Comparison between amitriptyline and placebo after 4 weeks of treatment for functional dyspepsia

	Amitriptyline group (n=43)	Placebo group (n=45)	95% CI of differences	P value
Mean frequency (SD), episodes per mo				
Month 1	3.88 (2.66)	2.4 (2.09)	0.385 to 2.404	0.007
Month 2	2.6 (2.40)	2.5 (2.26)	-0.84 to 1.129	
Median duration, n(%)				
Month 1				
<10 min	26 (60.5)	28 (62.2)		0.941
10-30 min	15 (34.9)	14 (31.1)		
30-60 min	2 (4.7)	3 (6.7)		
Month 2				
<10 min	28 (65.1)	31 (68.9)		0.728
10-30 min	14 (32.6)	12 (26.7)		
30-60 min	1 (2.3)	2 (4.4)		

Discussion

In our study the prevalence of functional dyspepsia in adolescents aged 12 to 18 years old was high (27.6%). The mean ages of subjects were 14.7 years in the amitriptyline group, and 14.9 years in the placebo group. We also found a higher incidence of dyspepsia in girls than in boys. Functional dyspepsia in children and adolescents requires attention. Adult treatments are not necessarily appropriate for children and adolescents. The prevalence of dyspepsia varies

between 3.5% and 27%.² A study in 449 Russian students aged 14 to 17 years showed that the incidence of functional dyspepsia was higher in adolescent girls than boys (27% vs. 16%, respectively).¹¹

Our study was conducted in a rural area with low parental incomes and educational levels. A Malaysian study reported that the incidence of recurrent abdominal pain was more common in school-aged children in rural areas compared to those in urban areas, and in those whose parents had low educational levels.¹²

A low dose of amitriptyline has been proposed as an alternative treatment for patients with functional dyspepsia. The daily dosage for children is 0.1 to 0.5 mg/kg body weight and 10 to 20 mg for adolescents. Therapeutic responses can be observed after 2 to 4 weeks of treatment.^{1,13,14} In our study, 10 mg and 20 mg of amitriptyline were given to subjects weighing <35 kg and ≥ 35 kg, respectively. Subjects were asked to take the medicine once daily at night to prevent alterations in school activities due to a drowsiness effect of amitriptyline. Therapeutic response was observed after 4 weeks of treatment.

The efficacy of amitriptyline might be explained by its anticholinergic properties. This action might reduce the pressure inside the stomach and its motility. Moreover, the analgesic action of this drug could be beneficial for functional dyspepsia patients whose threshold level of visceral sensitivity is lower (visceral hypersensitivity) compared to that of healthy subjects.¹⁵⁻¹⁷

Our study showed that amitriptyline and placebo were equally excellent for functional dyspepsia treatment, as both amitriptyline and placebo decreased the frequency and duration of functional dyspepsia. However, there were no significant differences in frequency or duration after treatment between the amitriptyline and placebo groups. A placebo effect can stimulate gastrointestinal condition in children. Further study on the effects of placebo in children with disruption functional gastrointestinal is needed to clarify the effect of placebo.¹⁸ Several studies have been published on the effects of placebo for treating migraines in children, a condition that also embraces a biopsychosocial model.¹⁹

The clinical benefits of amitriptyline were studied children and adolescents in California. Amitriptyline significantly reduced the frequency and severity of their recurrent abdominal pain.²⁰ A study on adults failing treatment with 4 weeks of famotidine were given amitriptyline for 4 weeks. In that study, amitriptyline was also effective for treating functional dyspepsia.²¹ In addition, another US study in 90 children aged 8 to 17 years who had functional gastrointestinal disorders, reported that amitriptyline and placebo both gave a good response to therapy, but with no significant difference between amitriptyline and placebo after 4 weeks of treatment.¹

A study in adult patients with irritable bowel

syndrome (IBS) showed that anxiety levels correlated with placebo analgesic effects. Some studies comparing the effects of placebo on migraines in adults and children showed a greater placebo effect in children than in adults.^{19,22} A meta-analysis of several clinical trials for placebo effect on IBS in adults found an average placebo response of 40%, with a range of 16% to 71%. The placebo effect was high because of the high expectations of subjects, as well as their parents and physicians during the study.²³

Our study had some limitations, such as lack of monitoring subjects' compliance in taking the medication. Monitoring was done only by counting the number of capsules that were returned to us. Also, the frequency and duration of the assessment were recorded only by subjects, not the researchers, and hence, prone to bias. More research is needed, especially regarding the benefits of placebo for treating functional dyspepsia.

In conclusion, amitriptyline and placebo are both able to reduce the frequency and duration of functional dyspepsia. However, amitriptyline is not more effective than placebo for functional dyspepsia treatment.

Conflict of Interest

None declared.

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