Natural Progression of Menstrual Pain in Nulliparous Women at Reproductive Age: An Observational Study

Chi-Mou Juang[1,2]*, Ming-Shien Yen[1], Huann-Cheng Horng[1], Chih-Yao Cheng[1], Chiou-Chung Yuan[1], Chia-Ming Chang[1]

[1]Division of General Gynecology, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, and [2]Institute of Epidemiology, College of Public Health, National Yang-Ming University School of Medicine, Taipei, Taiwan, R.O.C.

Background: Menstrual pain can be alleviated after childbirth. The purpose of this observational study was to evaluate the natural progression of menstrual pain among nulliparous women at their reproductive age.

Methods: A questionnaire-based study of perimenopausal women with a history of primary dysmenorrhea was performed. The study subjects were recruited between July 1, 2001 and June 30, 2005. Severity of menstrual pain was graded using a multidimensional scoring system.

Results: A total of 247 nulliparous women with primary dysmenorrhea were enrolled, and of these, 218 patients were eligible for analysis. Patients who had more frequent intercourse ($p = 0.016$), fewer associated systemic symptoms ($p = 0.028$), and use of oral contraceptive pills ($p = 0.039$) tended to have a higher chance of an improvement in dysmenorrhea after age 40. Multidimensional scoring distribution over chronologic age revealed that patients had significantly improved menstrual pain after 40 years of age.

Conclusion: For nulliparous women with primary dysmenorrhea, the severity of menstrual pain decreased significantly after age 40. More studies are needed to explore this phenomenon from a biochemical or molecular basis. [*J Chin Med Assoc* 2006;69(10):484–488]

Key Words: multidimensional scoring, nulliparous, primary dysmenorrhea

Introduction

Dysmenorrhea or menstrual cramping is one of the most common problems seen in women's health care. An estimated 50% of menstruating women are affected. The condition is most common between the ages of 15 and 25 years.[1] Dysmenorrhea can be further classified into primary and secondary dysmenorrhea. Primary dysmenorrhea is defined as pain during menses in the absence of an identifiable pathologic lesion, while in secondary dysmenorrhea, a macroscopic pelvic pathology is present. Primary dysmenorrhea is a disorder that affects 40–90% of the female population of reproductive age.[2–4] The etiology of primary dysmenorrhea is not precisely understood, but most symptoms can be explained by the action of uterine prostaglandins (PG), particularly PGF2α. Patients with primary dysmenorrhea have higher PG levels in the endometrium and menstrual blood.[5–8] It is a common belief that primary dysmenorrhea has its onset when ovulatory cycles begin, usually 6–12 months after menarche, peaks during the late teenage years and early twenties, then declines gradually with age.

To date, only 3 studies have examined the natural history of primary dysmenorrhea.[9–11] Unfortunately, the duration of longitudinal follow-up was relatively short in these studies. Moreover, parity had a strong influence on the natural history of primary dysmenorrhea, making the judgment of the impact of aging on primary dysmenorrhea more ambiguous. The purpose

*Correspondence to: Dr Chi-Mou Juang, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, R.O.C.
E-mail: cmjuang@yahoo.com.tw • Received: March 7, 2006 • Accepted: September 7, 2006

of this study was to evaluate the natural progression of menstrual pain among women with primary dysmenorrhea who had never had children.

Methods

Study design

We conducted an observational hospital-based study using data obtained from the Taipei Veterans General Hospital Dysmenorrhea Record Database. To exclude the effect of childbearing on dysmenorrhea, the targeted study subjects were perimenopausal nulliparous women with a history of primary dysmenorrhea. The study subjects were recruited between July 2001 and June 2005. The institutional review board of Taipei Veterans General Hospital approved this study. Study investigators were responsible for the identification of the original study subjects, and the research panel performed the case registration and data collection.

Patients and setting

The study subjects were nulliparous women over 40 years of age with a history of menstrual pain; when they presented to the gynecologic clinic, they had reported having had at least 1 episode of cramping pelvic pain during menstruation that made them try taking pain-relief drugs, or having had to be absent from school or work. If the patient met the inclusion criteria, a study investigator would invite her to participate in this study. At the initial interview, full medical and gynecologic histories were taken; physical examination was done and, if needed, ultrasonography was performed. Then, after obtaining their informed consent, patients were asked to complete a 25-item validated questionnaire. The questionnaire included items regarding demographic features, menstrual pattern, severity of menstrual pain across chronologic age (menarche, age 20, 30, 40 and 45), impact of dysmenorrhea on school attendance, job status, academic performance and social activities.

The severity of dysmenorrhea was measured by a multidimensional scoring system (MDS). The MDS was modified from that devised by Biberoglu and Berman.[12] The scoring denotes dysmenorrhea according to severity of dysmenorrhea as none (grade 0), mild (grade 1), moderate (grade 2) and severe (grade 3) based on pain, limited activities and medications taken as shown in Table 1. For simplicity of statistical analysis, classification of MDS was further collapsed into 2 categories, one for grade 0 and grade 1 and the other for grades 2 and 3.

Table 1. Multidimensional scoring of severity of dysmenorrhea

Grading	Working ability	Systemic symptoms	Analgesics
Mild	Rarely affected	None	Rarely required
Moderate	Moderately affected	Few	Required
Severe	Clearly inhibited	Apparent	Poor effect

Patients were excluded if they had cramping pelvic pain during menstruation that could be explained by local trauma, major pelvic trauma (e.g. traffic accident injury), specific food intake (e.g. icy food), severe medical disorder, or other clearly non-gynecologic pathology (e.g. inflammatory bowel disease, irritable bowel syndrome, acute cystitis, interstitial cystitis). As we intended to focus on primary dysmenorrhea, women who reported endometriosis, pelvic inflammatory disease or uterine fibroids were also excluded from the study.

Reassessment of dysmenorrhea

In order to maximize the reliability of data presentation, participants were asked to come back to complete the dysmenorrhea questionnaire again 1 month after the primary interview. If there was > 10% difference in the visual analog scale or 1 grade difference in the MDS between the 2 consecutive evaluations for an individual patient, then that patient underwent a repeated evaluation by a different study investigator.

Data analysis and statistical methods

Data were collected on standardized forms and encoded for computerized analysis using SPSS version 10.0 (SPSS Inc., Chicago, IL, USA) for Windows; flow chart was made using Visio 2003 (Microsoft Inc., Seattle, WA, USA), and figures were plotted using Sigmaplot 2001 (SPSS Inc.). Continuous variables were summarized by mean (range) or number (percent). Comparisons of MDS between different chronologic ages were made using repeated Mann–Whitney U test with Scheffe's correction or χ^2 test, as appropriate. Dependent categorical outcomes were analyzed with McNemar test, while dependent continuous outcomes were compared using the paired t test. Associations denoted as statistically significant were those that yielded a p value < 0.05, assuming a 2-sided alternative hypothesis.

Results

Study sample

A total of 247 patients were recruited. Of these, 29 patients were excluded due to the following reasons: 17 had confirmed pelvic pathologies; 2 were diagnosed with interstitial cystitis; 3 were diagnosed with irritable bowel syndrome; 1 had pelvic trauma history; 6 had incomplete data. The descriptive characteristics of the 218 eligible study subjects are shown in Table 2.

In order to find significant factors that correctly predicted improvement of dysmenorrhea with age, the study subjects were categorized into 2 groups. One was the improvement group and the other was the non-improvement group. The definition of improvement was that the patient had been relieved by at least 1 grade of MDS at age 40 as compared to age 20. At age 40, 136 patients (62.3%) had improvement in the severity of dysmenorrhea. There were no significant differences between the improvement and non-improvement groups with regard to patient age, menarche, menstrual duration, menstrual interval, and body mass index. The proportion of frequent intercourse (≥2 times/week) was higher in the improvement group (36.7%) versus the non-improvement group (23.1%; $p=0.016$). Patients who had fewer associated systemic symptoms tended to have improved dysmenorrhea after age 40. Patients who had ever used oral contraceptive pills for more than 5 years also tended to have improved dysmenorrhea compared to those who did not take pills.

Table 3 shows the distribution of MDS over chronologic age. There were significantly more nulliparous

Table 2. Baseline characteristics of study patients ($n=218$)*

	Improvement group ($n=136$)	Non-improvement group ($n=82$)	$p^{\dagger}$
Age (yr)	46 (45–51)	47 (45–52)	0.286
Age at menarche (yr)	12 (9–17)	13 (9–16)	0.658
Interval (yr)[‡]	0.8 (0–3)	1.2 (0–4)	0.471
Duration of menstruation (d)			0.192
1–5	115 (84.5)	68 (82.9)	
≥6	21 (15.6)	14 (17.1)	
Menstrual interval (d)			0.811
< 21	8 (5.9)	6 (7.3)	
21–35	116 (85.3)	68 (82.9)	
> 36	12 (8.8)	8 (9.7)	
Body mass index (kg/m^2)	23.1 (15.9–39.6)	23.5 (16.7–40.8)	0.818
Abortus in first trimester	0.8 (0–3)	0.9 (0–4)	0.713
Intercourse (times/wk)			0.016
≥2	50 (36.7)	19 (23.1)	
≤1	86 (63.2)	63 (76.9)	
Associated symptoms[§]			0.028
Yes	12 (8.8)	14 (16.9)	
No	124 (91.2)	68 (82.9)	
Use of oral contraceptive pills > 5 yr			0.039
Yes	28 (20.6)	6 (7.3)	
No	108 (80.9)	76 (93.4)	
Smoking			0.621
Yes	37 (27.2)	25 (30.4)	
No	99 (72.8)	57 (69.5)	
Alcohol user			0.818
Yes	32 (23.5)	21 (25.6)	
No	104 (76.4)	61 (74.4)	

**Data are presented as mean (range) or n (%), and sum of percentages may not total 100 due to rounding of figures; [†]Mann–Whitney U test with Scheffe's correction or χ^2 test as appropriate; [‡]interval between menarche and onset of dysmenorrhea; [§]reported symptoms associated with dysmenorrhea included fatigue, nausea, diarrhea, headache, backache, and epigastric pain.*

Table 3. Change in distribution of multidimensional scoring (MDS) over chronologic age*

Age distribution (yr)	Distribution of MDS†	*p*
< 20	Mild: 124 (56.8) Moderate: 67 (30.9) Severe: 27 (12.3)	Reference
20–29	None: 11 (5.0) Mild: 120 (55.0) Moderate: 61 (27.9) Severe: 26 (11.9)	0.338
30–39	None: 19 (8.7) Mild: 124 (56.9) Moderate: 54 (24.8) Severe: 21 (9.6)	0.173
≥ 40	None: 39 (17.9) Mild: 123 (56.4) Moderate: 42 (19.3) Severe: 14 (6.4)	0.036

**Data are presented as n (%), and sum of percentages may not total 100 due to rounding of figures; †estimated by McNemar's 2 × 2 test, with none + mild as one group, and moderate + severe as the other group.*

Table 4. Multiple stepwise logistic regression analysis of independent factors associated with improvement in dysmenorrhea after 40 years of age

Variable	OR	95% CI
Weight (BMI < 25 *vs.* ≥ 25)	2.16	1.49–2.85
Use of oral contraceptive pills (≥ 5 yr *vs.* < 5 yr)	1.83	1.27–2.49

BMI = body mass index; OR = odds ratio; CI = confidence interval.

women with primary dysmenorrhea who experienced improvement in menstrual pain after age 40.

Table 4 presents the logistic regression analysis of factors associated with improvement of dysmenorrhea among nulliparous women after age 40. Two independent factors were identified: normal weight and oral contraceptive pill user were the 2 factors that predicted improvement of dysmenorrhea.

Discussion

The present study found that women with primary dysmenorrhea who had never had children had a chance of their menstrual pain improving after age 40. In contrast, a longitudinal study of young women between the ages of 19 and 24 by Sundell et al[13] showed that the severity of dysmenorrhea only decreased in women who had children during those 5 years, and was unchanged in women who remained nulliparous, had a miscarriage or had an abortion. Apparently, the length of follow-up is the key factor in the outcome difference between these 2 studies. A study by Weissman et al[9] also found that age had a significant effect on the severity of dysmenorrhea, after adjusting for parity, indicating that older women are more likely to experience a decrease in the severity of dysmenorrhea, independent of childbearing. However, childbearing was clearly the more influential factor in this analysis. In contrast, some studies found that childbearing had no significant impact on improving severity of dysmenorrhea, after controlling for age or age and smoking.[14,15] The natural progression of menstrual pain is, thus, a very interesting issue and deserves further study to investigate the underlying pathophysiologic mechanisms.

There have been several studies on the impact of oral contraceptive pills on the severity of dysmenorrhea. The results indicate that oral contraceptive pills can statistically and clinically significantly reduce the incidence and severity of dysmenorrhea, and its impact on daily activities.[16–19] Our study further confirmed that oral contraceptive pills had a positive impact on the severity of dysmenorrhea, on the condition that they were used for longer than 5 years. Even in non-current users, oral contraceptive pills can still ease the severity of dysmenorrhea after age 40, implying that they may be able to modify pain-triggering factors.

Our study also found that nulliparous women with primary dysmenorrhea who had regular sexual intercourse at a frequency of 2 or more times per week could significantly diminish the severity of menstrual pain after age 40. This phenomenon is hard to explain, and deserves further in-depth investigation. Some studies suggest that women who smoke, drink alcohol, or who began menstruation early in life (before age 11) have an increased risk of dysmenorrhea. On the contrary, our results did not corroborate such findings. Owing to the observational nature of our study, the results may not be so valid. Further controlled trials are needed to resolve these questions. As for body weight, the results of our report parallel those of previous studies, indicating that overweight women have twice the risk of non-improvement of menstrual pain after age 40.

Dysmenorrhea-associated symptoms include fatigue, nausea, diarrhea, headache, backache, and epigastric pain. The current study demonstrated that there was significant negative correlation between the presence of dysmenorrhea-associated symptoms and the improvement of dysmenorrhea at age 40. Viewed from another angle, if a woman with primary dysmenorrhea had no associated symptoms, she would more easily get relief from dysmenorrhea at the age of 40

than women who had associated symptoms. We thus hypothesize that among women with primary dysmenorrhea who had more associated systemic symptoms, the etiologic factor(s) that induced the menstrual pain were different from those in patients with fewer associated systemic symptoms.

The major defect of the current study is that the analysis was largely based on retrospective data. Therefore, recall bias could be a concern. We had each patient undergo 2 evaluations 1 month apart. If there was > 10% discrepancy between the 2 consecutive evaluations, a third evaluation was conducted. Thus, the data were more reliable. Of course, a prospective longitudinal survey would have made the study results more convincing, but such a study takes more time and effort.

In summary, nulliparous women with primary dysmenorrhea may be relieved from menstrual pain after the age of 40 years, especially in those who had frequent sexual activity, those with fewer associated systemic symptoms, and those who had used oral contraceptive pills for longer than 5 years. More in-depth studies are needed to explore the interrelationships among these factors.

References

1. Klein JR, Litt IF. Epidemiology of adolescent dysmenorrhea. *Pediatrics* 1981;68:661–4.
2. Dmitrovic R, Peter B, Cvitkovic-Kuzmic A, Strelec M, Kereshi T. Severity of symptoms in primary dysmenorrhea—a Doppler study. *Eur J Obstet Gynecol Reprod Biol* 2003;107:191–4.
3. Milsom I, Sundell G, Andersch B. The influence of different combined oral contraceptives on the prevalence and severity of dysmenorrhea. *Contraception* 1990;42:497–506.
4. Jamieson DJ, Steege JF. The prevalence of dysmenorrhea, dyspareunia, pelvic pain, and irritable bowel syndrome in primary care practices. *Obstet Gynecol* 1996;87:55–8.
5. Lundstrom V, Green K. Endogenous levels of prostaglandin F2alpha and its main metabolites in plasma and endometrium of normal and dysmenorrheic women. *Am J Obstet Gynecol* 1978; 30:640–6.
6. Chan WY, Dawood MY, Fuchs F. Relief of dysmenorrhea with the prostaglandin synthetase inhibitor ibuprofen: effect on prostaglandin levels in menstrual fluid. *Am J Obstet Gynecol* 1979; 35:102–8.
7. Nigam S, Benedetto C, Zonca M, Leo-Rossberg I, Lubbert H, Hammerstein J. Increased concentrations of eicosanoids and platelet-activating factor in menstrual blood from women with primary dysmenorrhea. *Eicosanoids* 1991;4:137–41.
8. Bieglmayer C, Hofer G, Kainz C, Reinthaller A, Kopp B, Janisch H. Concentrations of various arachidonic acid metabolites in menstrual fluid are associated with menstrual pain and are influenced by hormonal contraceptives. *Gynecol Endocrinol* 1995; 9:307–12.
9. Weissman AM, Hartz AJ, Hansen MD, Johnson SR. The natural history of primary dysmenorrhoea: a longitudinal study. *Br J Obstet Gynaecol* 2004;111:345–52.
10. Sundell G, Milsom I, Andersch B. Factors influencing the prevalence and severity of dysmenorrhoea in young women. *Br J Obstet Gynaecol* 1990;97:588–94.
11. Harlow SD, Park M. A longitudinal study of risk factors for the occurrence, duration and severity of menstrual cramps in a cohort of college women. *Br J Obstet Gynaecol* 1996;103: 1134–42.
12. Biberoglu KO, Behrman SJ. Dosage aspects of danazol therapy in endometriosis: short-term and long-term effectiveness. *Am J Obstet Gynecol* 1981;139:645–54.
13. Vercellini P, Aimi G, Busacca M, Apolone G, Uglietti A, Crosignani PG. Laparoscopic uterosacral ligament resection for dysmenorrhea associated with endometriosis: results of a randomized, controlled trial. *Fertil Steril* 2003;80:310–9.
14. Messing K, Saurel-Cubizolles MJ, Bourgine M, Kaminski M. Factors associated with dysmenorrhea among workers in French poultry slaughterhouses and canneries. *J Occup Med* 1993;35: 493–500.
15. Pullon S, Reinken J, Sparrow M. Prevalence of dysmenorrhea in Wellington women. *N Z Med J* 1988;101:52–4.
16. Callejo J, Diaz J, Ruiz A, Garcia RM. Effect of a low-dose oral contraceptive containing 20 microg ethinylestradiol and 150 microg desogestrel on dysmenorrhea. *Contraception* 2003;68: 183–8.
17. Vercellini P, Frontino G, De Giorgi O, Pietropaolo G, Pasin R, Crosignani PG. Continuous use of an oral contraceptive for endometriosis-associated recurrent dysmenorrhea that does not respond to a cyclic pill regimen. *Fertil Steril* 2003;80: 560–3.
18. Hendrix SL, Alexander NJ. Primary dysmenorrhea treatment with a desogestrel-containing low-dose oral contraceptive. *Contraception* 2002;66:393–9.
19. Harel Z. A contemporary approach to dysmenorrhea in adolescents. *Pediatr Drugs* 2002;4:797–805.