Dysmenorrhea in Young People: Experiences from a Tertiary Centre with a focus on Conservative Management

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Running Title: Dysmenorrhoea in Young People**Abstract***Aim*

To describe the characteristics, management, and outcomes of a cohort of young people with dysmenorrhea presenting to a tertiary adolescent gynaecology service, managed primarily with medical interventions.

Methods

A retrospective cohort study was conducted at the Royal Children's Hospital in Melbourne, Australia. Data were collected from medical records of patients presenting with dysmenorrhea and/or pelvic pain.

Results

Of 154 patients, mean age of presentation was 15.7 years (SD=2.2) and mean duration of pain was 14.9 months (SD=10.8). Regular cycles were reported by 64.5%, and heavy menstrual bleeding (HMB) in 67.8%. Patients self-reporting HMB reported less pain on the day prior to menses than those not reporting HMB ($p<0.005$). At follow-up, therapeutic interventions included nonsteroidal anti-inflammatory drugs, tranexamic acid, and cyclic or continuous combined oral contraceptive pills. Laparoscopies were undertaken in 12 (8.1%) patients, with normal findings in 8 (66.7%). Secondary dysmenorrhea was identified in 10 patients: of these, endometriosis was identified in one patient and unilateral obstructive Müllerian anomalies in six. Overall, 92.2% of patients had improvement in symptoms after treatment.

Conclusion

Laparoscopy and endometriosis rates in patients presenting to a tertiary centre were lower than previously reported, with most patients achieving symptom improvement without laparoscopy.

Keywords: adolescent, dysmenorrhea, endometriosis, laparoscopy, pelvic pain, prostaglandin

Definitions

The World Health Organization defines adolescents and young people as those between the ages of 10 and 19, and 10 and 24 respectively. In our manuscript, we have included patients between the ages of 9 and 22, referred to as “young people.”

Introduction

Dysmenorrhea is common in young people, with reported rates of 20 to 90%.^{1,2} It is classically described as either primary or secondary.

Primary dysmenorrhea is thought to occur in ovulatory cycles²: the fall in progestogens results in an inflammatory process which provokes endometrial shedding by way of the production of inflammatory mediators in the endometrial tissue. These inflammatory mediators incite a range of associated local and systemic symptoms that occur just prior to or during menstruation.^{1,2}

Nonsteroidal anti-inflammatory drugs (NSAIDs) and the combined oral contraceptive pill (COCP) are recommended as first line treatments for patients presenting with primary dysmenorrhea and associated symptoms.¹

Secondary dysmenorrhea, where underlying pathology is present, has been described in approximately 10% of young patients with dysmenorrhea; endometriosis is the most commonly identified underlying cause.^{2,3} Of those who have failed first line management with NSAIDs and COCP, 62% (range 25-100%) have been found to have visually proven endometriosis at laparoscopy, with reported rates of up to 73.5% in patients with severe dysmenorrhea.⁴

Laparoscopy has thus been recommended as a means of identifying endometriosis in patients whose symptoms persist despite the use of NSAIDs and COCP beyond 3-6 months.²⁻⁷

Other causes of secondary dysmenorrhea in younger patients include Müllerian anomalies, ovarian masses, and pelvic inflammatory disease.² Obstructed reproductive tract anomalies have been reported in three to eight percent of adolescents with dysmenorrhea presenting to specialist hospital clinics.^{6,8}

Whilst laparoscopy is still considered the gold standard for the diagnosis of endometriosis, recommending the early use of laparoscopy in adolescents with dysmenorrhea raises significant concerns. Several studies have demonstrated a recurrence of pain within 12-18 months, with many young women then undergoing repeat surgical procedure(s).^{9,10} Predictors for repeat laparoscopy for pelvic pain include younger age and previous pelvic laparoscopy.^{11,12} A placebo effect of up to 30% has been reported in the literature, whereas up to 20% of women describe no improvement in symptoms.¹³ Medical treatment is proven to be effective for symptom control in adolescents with dysmenorrhea¹⁴⁻¹⁶ and recently has been shown to be associated with a reduction in size of endometriotic nodules in cases of moderate to severe rectovaginal endometriosis.¹⁷ Furthermore, there is a cohort of women who develop pain syndromes and myofascial pain following surgery.^{1,18} Finally, there is evidence that the pain sensitivity threshold of women with dysmenorrhea is lower than the pain sensitivity threshold of women without dysmenorrhea, regardless of the presence or absence of endometriosis.¹⁹

Our study therefore aims to clarify the characteristics of dysmenorrhea in young patients and to determine if adequate symptom control is achievable with a predominantly medical approach, with use of laparoscopy limited to patients with ongoing pain despite attempts to achieve complete suppression of menses.

Methods

Patients presenting with dysmenorrhea to the Department of Paediatric and Adolescent Gynaecology at the Royal Children's Hospital (RCH) in Melbourne, Australia between 1997 and 2004 were identified from the outpatient record database. All patients had been referred by a primary care practitioner (family physician or paediatrician). Patients who were referred with pain but whose primary diagnosis was non-gynaecologic (for example: abdominal wall trigger points, irritable bowel syndrome, bladder pain syndrome), were excluded only when pelvic pain or dysmenorrhea was not a substantial component of their symptoms. However, patients in whom pelvic pain or dysmenorrhea was the chief symptom in their referral or presentation, even in the setting of other conditions, were still included. ICD codes for genital tract anomalies for the same period were also identified and cases where unilateral obstruction was present, but menstruation could occur from one functional side of the Müllerian system, were included. A retrospective chart review was performed and data extracted regarding age of menarche, age at onset of dysmenorrhea, age at presentation to our clinic, associated symptoms, pattern of menses, school missed due to dysmenorrhea, medications trialled prior to referral and those prescribed by the specialist adolescent gynaecologists, investigations prior to referral and during attendance at the clinic, operative procedures and findings, and outcomes at subsequent clinic appointments. All patients were seen in consultation by 1 of 3 consultant paediatric gynaecologists and/or 1 fellow under supervision. A standard approach to management of dysmenorrhea was employed (Figure 1). This was tailored to individual patient's medication contraindications and patient preferences at the discretion of the treating gynaecologist. Laparoscopies were performed by 1 of 3 consultant gynaecologists specializing in paediatric & adolescent gynaecology. HMB was documented as self-reported heavy menstrual loss. A regular menstrual cycle was defined as 25 to 35 days. Information regarding socioeconomic status was gained by utilizing the postcode related data available from the Australian Bureau of Statistics for Socio Economic Information for Area.²⁰

All data analysis was performed using Stata 11. Chi Square, Fisher's exact and logistic regression were used to test correlation. The project was undertaken with RCH Human Research and Ethics approval (CA29080) as a clinical audit project and as such did not require patient consent.

Results

A total of 154 patients with dysmenorrhea or pelvic pain were identified, accounting for 9% of all outpatient visits in this time period. Age of presentation was between 9 and 22 years (mean 15.7, SD=2.2). Age at menarche was between 9 and 14 years (mean 11.8, SD=1.3) and mean interval from menarche to presentation was 3.8 years (SD=1.8). Mean duration of pain was 14.9 months (SD=10.8).

School absenteeism was only recorded in a small subset of girls and therefore was not included in analysis.

An uneven distribution of socioeconomic background was found. Although the majority of patients fell within the middle socio-economic bracket, three-quarters were noted to reside in socio-economic areas above the 50th percentile.

Self-assessment of menstrual flow was recorded in 143 patients: of these, 97 (67.8%) reported HMB and 28 (19.5%) reported the presence of clots in menstrual loss, although this was not further quantified. Other than presence of clots, there was no difference in baseline characteristics of patients reporting and not reporting HMB (Table 2).

The menstrual cycle pattern was recorded in 138 (89.6%) patients. Of these, regular cycles were reported in 89 (64.5%).

The exact timing and pattern of pain was noted in 126 (81.8%) patients. In 84.9%, the pain was most severe on days 1 and 2 of menses; 38.1% reported pain on days 3 to 4, and 15.1% on days 5 to 6. Pain began the day prior to menses in 54.7% and between two and seven days before menses in 23.8%.

Patients reporting HMB (n=97) experienced significantly less pain on the day prior to menses than those without HMB (n=28) ($p<0.005$). There was no association between duration of menses and HMB, and no significant difference in pain pattern between girls reporting regular cycles and those reporting irregular cycles. (Table 2)

Associated symptoms were recorded in 148 patients: nausea (39.9%), diarrhoea (33.1%), headaches (32.4%), tiredness (28.4%), back pain (27.7%), vomiting (26.4%), irritable mood (14.9%), syncope (12.8%), anorexia (10.1%), dizziness (8.8%), constipation (7.4%) and bloating (4.7%). Eleven (7.4%) patients did not report any associated symptoms. (Table 1)

There was a significant correlation between nausea and other symptoms: vomiting ($p<0.005$), diarrhoea ($p<0.05$), headaches ($p<0.005$) and tiredness ($p<0.01$). Overall, 70.8% reported nausea, vomiting, diarrhoea, dizziness or feeling faint, with 29.8% reporting 3 or more of these symptoms. Of the patients who did not report any of this cluster of symptoms, 74.4% had HMB.

Medical Management

A range of pain management approaches had been trialled by most patients prior to referral: NSAIDs (71.4%), cyclic COCP (23.1%), alternative therapies (8.2%), continuous COCP (5.4%), oral progestogens (4.8%), tranexamic acid (0.7%) and depot medroxyprogesterone acetate (DMPA) (0.7%). Twenty patients (13.6%) reported no medications or interventions prior to their specialist consultation.

During the first consultation, patients were prescribed or given instructions for optimal use of NSAIDs (51.4%), cyclic COCPs (26.4%), continuous COCPs (20.8%), tranexamic acid (11.5%), alternative medicine (6.8%) and/or oral progestogens (2.7%).

During the course of the subsequent consultations, NSAIDs were prescribed for 60.1%, continuous COCPs for 49.3% and cyclic OCPs for 46.6%. Other management, used in combination or alone, included tranexamic acid (20.7%), oral progestogens (12.6%), alternative

treatment (8.1%), DMPA (4.5%), etonorgestrel implant (1.8%) and levonorgestrel intrauterine system (IUS) (1.8%).

Surgical management

Laparoscopy

Four patients had undergone laparoscopy prior to referral to our clinic: three were reportedly normal and one had findings of mild endometriosis. This patient had not trialled any medical treatments pre-operatively. Twelve patients (8.1%) underwent laparoscopy for further investigation, including one patient who underwent repeat laparoscopy. Indication for laparoscopy was ≥ 12 months of persistent pain despite trial of $\geq$ two hormonal medications (Figure 1). Eight of these patients had ongoing pain despite the use of continuous COCP. Abnormal findings at laparoscopy were noted in four patients: presence of minor adhesions in two patients, ovarian cyst in one patient and histologically proven mild endometriosis in one patient. No pelvic pathology was found in the remaining eight cases. The patient who was found to have mild endometriosis had not achieved menstrual suppression despite medical management, including use of GnRH-analogue.

Correction of anomalies

Six patients (3.3%) were identified with uterine didelphys, obstructed hemivagina with ipsilateral renal agenesis. All were managed operatively with excision of the vaginal septum. None of these patients underwent laparoscopy. The mean age at presentation of this group was 14.2 years (SD=2.5). All had resolution of pain following correction of the anomaly.

Follow-up

Of the 154 patients in the study, 38 (24.8%) did not return for clinical follow-up. Of these, 20 had not used any interventions or medications prior to their first consultation.

Of the 115 (74.7%) patients who presented for follow-up, median follow-up was 11 months (IQR: 3-26). Median and mean number of clinic visits were 3 and 3.9 (SD=3.52) respectively.

Symptoms were reported to be *resolved* or *well-controlled* following medical/surgical intervention by 59.7% of patients, while 32.2% were *somewhat improved*. These were subjective measures documented at follow-up visits. Thirteen patients (8.4%) reported ongoing dysmenorrhea. (Figure 2)

Discussion

This study population represents a group of young patients with dysmenorrhea referred by primary care practitioners, paediatricians and other general gynaecologists to a specialised paediatric and adolescent gynaecology clinic at a tertiary paediatric hospital. The cohort in this study represents patients referred with pelvic pain or dysmenorrhea, but excludes those who were found to have alternative non-gynaecological causes for their pelvic or abdominal-pelvic pain such as abdominal wall trigger points, irritable bowel syndrome or bladder pain syndrome. The mean age of presentation and of menarche of our population is similar to other reports of young patients with dysmenorrhea.²¹⁻²³ Although some studies have suggested that early menarche is a risk factor for dysmenorrhea¹, this is not supported by our findings. Reports have previously suggested that patients with higher socioeconomic status are at higher risk of dysmenorrhea.²⁴ Our study is congruent with this observation; however, we hypothesize that this may simply reflect improved access to medical services and/or improved health literacy. Primary dysmenorrhea has been reported to occur with ovulatory cycles, rather than immediately after menarche, due to an increase in prostaglandin production triggered by a fall in progestogens.¹ More recently, this theory has come into question secondary to a lack of difference in dysmenorrhea rates between ovulating and non-ovulating patients.²⁵ One third of

our adolescent dysmenorrheic patients reported irregular cycles, with anovulation likely to be the cause, further challenging the link between ovulation and the subsequent fall in progestogens as the key trigger to prostaglandin production. The symptom cluster of nausea, vomiting, diarrhoea, headaches and dizziness, found in 70.8% of our study cohort, has been reported by others to be associated with primary or prostaglandin-induced dysmenorrhea¹, implying that prostaglandin release and the inflammatory process of menstrual shedding are still present.

Reports on the association between HMB and dysmenorrhea are mixed, with rates of 10.8% to 85.6%.^{21, 26} As the reliability of self-reports of menstrual loss is questionable, particularly in this young population²⁷, and no standardized bleeding assessment tool was used, the significance of this finding is unclear. Nevertheless, our data suggest the possibility of a different pain pattern in girls self-reporting HMB, as they appear to have less systemic prostaglandin-associated symptoms and less pain on the days prior to menses when compared to those who did not report HMB. Approaches aimed at reducing menstrual blood loss, such as tranexamic acid, may be useful in this sub-group. Further studies are required to clarify this possible bimodal pattern.

It has been recommended that laparoscopy be undertaken for investigation of dysmenorrhea where NSAIDs and the COCP have failed.⁷ In fact, studies on dysmenorrhea in adolescents have tended to specifically report on findings in this population^{6,23,28}, rather than on a cohort presenting with dysmenorrhea or pain. The total laparoscopy rate in our study (including four patients in whom laparoscopy was undertaken prior to referral to our service) was only 10.4%. It is our routine practice to aim for complete menstrual suppression for six months prior to laparoscopy for dysmenorrhea. We hypothesize that cyclic use of the COCP with subsequent endometrial shedding results in the release of prostaglandins and inflammatory cytokines during the hormone-free-interval, permitting the propagation of pain induced by these substances.

Our routine use of continuous COCP may thus account for both the low laparoscopy rate and the low endometriosis rate found in our population. Of the patients who had persistent symptoms despite medical management, only one was found to have endometriosis; menstrual suppression had not been successfully achieved in this patient. Overall, 92.2% of our cohort had self-reported improved or resolved symptoms despite a very low surgical intervention rate. Six (3.3%) of our patients had a hemi-obstructed congenital anomaly. These patients had resolution of symptoms following primary corrective surgery without the addition of laparoscopy. Overall, 10 (6.5%) of our patients were found to have a secondary cause of dysmenorrhea. This is much lower than that reported by other studies and may partly reflect our low laparoscopy rate and possible undiscovered secondary causes. Additionally, the rate of positive findings (33.3%) amongst those who did undergo laparoscopy is lower than reported by others. However, the 13 patients who reported their symptoms had not improved or were not well controlled despite receiving medical management may increase this number were they to undergo laparoscopy.

We acknowledge that there are several limitations to our study. Firstly, our inclusion and exclusion criteria resulted in a population of patients whose symptoms were predominately limited to dysmenorrhea and/or pelvic pain without the presence of other pain syndromes. Thus, the results cannot be extrapolated to patients with these co-morbid conditions. Equally, our findings may be valuable to those patients presenting with chiefly isolated dysmenorrhoea or pelvic pain. Additionally, 38 (24.8%) of our patients did not attend follow-up after their first visit to our clinic. Of these were 20 who had not undertaken any interventions prior to their first consultation and thus the information given and simple advice may have resolved their concerns. It is possible that the remaining 18 patients had improvement in their symptoms after initial medical management, and therefore did not feel the need to return, or alternatively were dissatisfied with initial treatment and thus sought further management elsewhere. Finally, several of our measures, including presence of HMB and degree of improvement in symptoms,

were subjective and descriptive, thus obtaining quantitative results was not possible in these instances.

Conclusion

In our study, most patients were successfully treated with medical management without the need for surgical intervention, and we found a smaller proportion of patients with secondary dysmenorrhea from obstructive anomalies and endometriosis than previously reported. We propose that in patients presenting with dysmenorrhea and/or pelvic pain, complete menstrual suppression be included in a trial of medical therapy prior to moving onto considering surgical investigation. The long-term follow-up of our cohort has been reported in a separate study and sheds further encouraging, positive light on this conservative approach to dysmenorrhea in young patients.¹⁴

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Legends for Tables & Figures

Table 1. Patient descriptors and associated symptoms

Table 2. Characteristics of patients reporting or not reporting HMB at presentation

Figure 1. Royal Children's Hospital Paediatric & Adolescent Gynaecology protocol for management of dysmenorrhoea. *a. offered to all patients with dysmenorrhoea, b. offered to all patients with HMB. c. oral, intramuscular, subdermal, or intrauterine.*

Figure 2. Symptom control at the time of follow-up

Figure 1. Royal Children's Hospital Paediatric & Adolescent Gynaecology protocol for management of dysmenorrhoea. *a. offered to all patients with dysmenorrhoea, b. offered to all patients with HMB. c. oral, intramuscular, subdermal, or intrauterine.*

Figure 2. Symptom control at the time of follow-up

Demographics (N=154)	Mean (SD)
Age of presentation (y)	15.7 (2.2)
Age of menarche (y)	11.8 (1.4)
Time from menarche to presentation (y)	3.8 (1.8)
Duration of pain (m)	14.9 (10.8)
Cycle regularity (N=138)	n (%)
Regular (25-35d)	89 (64.5)
Irregular	49 (35.5)
Menstrual flow (N=143)	n (%)
HMB	97 (67.8)
Clots in menstrual loss	28 (19.5)
Associated symptoms (N=148)	n (%)
Nausea	59 (39.9)
Diarrhoea	49 (33.1)
Headache	48 (32.4)
Tiredness	42 (28.4)
Back pain	41 (27.7)
Vomiting	39 (26.4)
Irritable mood	22 (14.9)
Syncope	19 (12.8)
Anorexia	15 (10.1)
Dizziness	13 (8.8)
Constipation	11 (7.4)
Bloating	7 (4.7)
No associated symptoms	11 (7.4)

Table 1. Patient descriptors and associated symptoms

	no HMB (n=46)	HMB (n=97)	
	mean (SD)	mean (SD)	p-value
age of presentation	15.8 (2.4)	15.7 (2.1)	0.84
age of menarche	11.8 (1.1)	11.7 (1.4)	0.74
	n (%)	n (%)	p-value
regular cycles (5)	27 (61.4)	62 (66.0)	0.6
alternate medications	5 (10.9)	7 (7.2)	0.46
NSAIDs	35 (76.1)	67 (69.1)	0.39
TXA	0 (0.0)	1 (1.0)	0.49
progesterone	1 (2.2)	6 (6.2)	0.3
DMPA	0 (0)	1 (1.0)	0.49
cyclic OCP	10 (21.7)	22 (22.7)	0.9
continuous OCP	2 (4.4)	6 (6.2)	0.66
etonorgestrel implant	0 (0)	0 (0)	1
levonorgestrel IUD	0 (0)	0 (0)	1
clots	1 (2.2)	29 (29.9)	<0.01

Table 2. Characteristics of patients reporting or not reporting HMB at presentation

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