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Comparing Effectiveness of Intrauterine Devices Versus Oral Contraceptives for Management of Dysmenorrhea

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by

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Abstract

The purpose of this research and systematic literature review is to determine if oral contraceptives or intrauterine devices are more effective in the treatment of dysmenorrhea pain. It is estimated that at least 50% of women worldwide live with dysmenorrhea and there is very little research determining what the best treatment options are for it. The main treatment recommended by health care providers for dysmenorrhea are non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen. However, this treatment option may not provide the relief that women with this condition need. This review used three main databases, including PubMed, Embase, and Clinical Key in order to find pertinent research and articles. A variety of key words were used in the search, such as dysmenorrhea, oral contraceptives, and intrauterine devices. The studies found were then narrowed down by excluding studies older than 2011 and including relatively pertinent studies that were either randomized controlled trials, clinical trials, open-label, parallel group studies, interventional studies, observational studies, secondary analyses, or pilot studies. Out of the studies included in this review, only one compared the effectiveness of oral contraceptives and intrauterine devices. Each study reviewed showed that oral contraceptives and intrauterine devices were safe and effective options, but in a single head-to-head study, it was determined that intrauterine devices were superior in relieving dysmenorrhea. The evidence showed that intrauterine devices were often not as well tolerated and resulted in discontinuation of use due to the side effects. Despite the results of the article, more research needs to be conducted prior to making a definitive decision on the best treatment method for dysmenorrhea.

Keywords: Dysmenorrhea, oral contraceptives, intrauterine devices

Introduction

Dysmenorrhea is a term used to describe pain associated with menses. Multiple studies indicate that dysmenorrhea affects at least 50% of menstruating women worldwide. There are two categories of dysmenorrhea, primary and secondary. Primary dysmenorrhea does not have a known pathology or etiology of the pain elicited during the onset of menstruation. Secondary dysmenorrhea does have a known cause contributing to the patient's pain, such as endometriosis, adenomyosis, fibroids, and many more. The current treatment of this type of pain is typically with non-steroidal anti-inflammatory drugs (NSAIDs), such as naproxen or ibuprofen. However, this may not be an option due to being contraindicated for other comorbidities or may not be an effective pain control measure in some patient populations. The purpose of this literature review is to explore other treatment options by comparing the use of either oral contraceptives or intrauterine devices in the treatment of dysmenorrhea.

Statement of Problem

Women's health is generally under researched and often times women are undertreated due to this lack of studies. For example, with menstrual pain, women are often told that it is normal, and they simply need to take NSAIDs. For this reason, women will rarely seek medical advice for their ailments. It is important for a provider to be able to discuss with a patient the etiologies of their pain, the tests required to aid in the diagnosis of their pain, and have a general understanding of the treatment options that exist in order to help alleviate the pain women are enduring associated with their menses. It is also important for providers to not ignore a patient's pain by labeling it as a normal part of the patient's menstrual cycle. Menses are not supposed to be painful, and women should not have to live with the pain they experience. With how much of

the population suffers from dysmenorrhea, there should be more studies and treatment options for it.

Research Question

In patients with dysmenorrhea, are oral contraceptives or hormonal intrauterine devices more effective at pain control?

Methods

A comprehensive literature review was conducted using various online databases. This review used current research findings from PubMed, Embase, and ClinicalKey. Both keywords and mesh terms were used within these databases in order to find appropriate research pertaining to the topic of dysmenorrhea. The search began with using broad words such as dysmenorrhea, oral contraceptives, and intrauterine devices. This left many studies that needed to be narrowed down by selecting certain criteria. The articles chosen for this literature review were conducted within the past 11 years to ensure the information is up to date, they were peer-reviewed, and included randomized controlled trials, clinical trials, open-label, parallel group studies, interventional studies, observational studies, secondary analyses, or pilot studies. Various studies were excluded if they did not involve factors that addressed the research question regarding treatment of dysmenorrhea with oral contraceptives or intrauterine devices. These studies were furthermore searched for discussing quality of life, which is a factor of pain control for dysmenorrhea. There was very little research conducted with regards to comparing these treatments for dysmenorrhea. In order to find enough articles pertinent to this literature review, the topic was broadened to include secondary dysmenorrhea in addition to primary dysmenorrhea.

Literature Review

Effectiveness of oral contraceptives for dysmenorrhea

Al-Jefout and Nawaiseh (2016) conducted a prospective, open-label, nonrandomized study evaluating the efficacy of treating dysmenorrhea with a 5mg continuous norethisterone acetate (NET-A) versus a cyclical combined oral contraceptive pill (COC) which consists of 3mg drospirenone and 20 μg estradiol. The population included 38 participants who were all young adult Jordanian woman aged 18-23 years old with dysmenorrhea for at least 6 months. Between these 38 individuals, there were 20 in the NET-A group (N group) and 18 in the COC (P group). They were given the choice of which treatment they wanted to receive and then the study began when the desired sample size was achieved.

Inclusion criteria for this study required the subjects to have a history of severe dysmenorrhea associated with at least two conditions of cyclical use of analgesics for pain control and a history of negative effects dysmenorrhea has on work or school. They also required a recent history of regular menstrual cycles and a BMI between 18-30. Another factor that these participants had in common, although not required for inclusion criteria, was that none of them were sexually active. Exclusion criteria for this study include a history of high blood pressures, clotting disorders, irregular periods, and a history of fibrocystic breast disease, lumps, nodules, or abnormal mammograms. Physical exams and transabdominal ultrasounds were also performed and women who were found to have endometriomas or abnormal ovarian pathology were excluded from the study.

In order to assess the participants between the 3-month and 6-month follow ups, they were given menstrual cycle diaries to record everything regarding their periods, to include presence, absence, and severity of dysmenorrhea, in addition to any symptoms, side effects, and analgesic

use. During the 3 and 6- month evaluations, participants were asked to complete a detailed 25-item self-administered questionnaire that asked about presence of pain, irregular bleeding episodes, breast tenderness, headaches, and need for analgesics. This study also utilized the 10-point visual analog scale (VAS) at the start of the study, 3 months in, and 6 months in to evaluate the efficacy of these treatments for dysmenorrhea.

At the start of the study, the VAS scores, mean (± SD) in group N and group P were 6.70 ± 1.17 and 6.89 ± 1.13 (p= 0.618), respectively. The results were similar between the N and P groups at both the 3 month and 6 month follow ups. At 3 months, the VAS scores showed 1.30 ±1.22 for the N group and 1.28 ±0.83 for the P group (p= 0.218). Finally, at the 6 month follow up, the VAS scores were 1.30 ±1.22 for the N group and 1.28 ± 0.83 for the P group (p= 0.949).

The most common side effects noted by both groups were bloating or swelling. The N group had 10 participants report these side effects while the P group only had 2 participants report them. The difference between the two groups was statistically significant with a p value of 0.010. Other side effects reported that did not show any statistical significance included mood changes, spotting, breakthrough bleeding, headaches, irritability, and breast tenderness. The results also showed that analgesic use decreased significantly throughout the study. At the start of the study, 20% of the N group and 44% of the P group used analgesics (p = 0.006). By 3 months only 5% of the N group and 17% of the P group were using analgesics (p = 0.019). By the end of the study, no participants were using analgesics for symptom relief. The findings from this study indicate that both continuous norethisterone acetate and cyclical 3 mg drospirenone/ethinyl estradiol 20 μg are effective in reducing dysmenorrhea pain, bleeding, and analgesic use. One of the strengths of this study was that the population had a significant inclusion and exclusion criteria, which leaves little to debate. Patients were very similar to one another, and they all had

primary dysmenorrhea. Although this study was a good source, there were many weaknesses. These include a small sample size, there was no control group, the groups were not randomized, and participants knew which treatment they were receiving (Al-Jefout & Nawaiseh 2016).

El Taha et al. (2021) conducted a randomized, double-blinded, parallel clinical trial comparing the efficacy of dienogest, a progestin only oral contraceptive, to the combined oral contraceptive (COC) Yasmin for control of endometriosis-associated pelvic pain. The population of this study consisted of 70 women with a histologically confirmed diagnosis of endometriosis, dysmenorrhea for at least six months, be 20 to 45 years of age, have regular menstrual cycles, a baseline endometriosis-associated pelvic pain VAS score of ≥ 4, presence of one or more subjective symptoms during menstruation and lastly, the presence of one or more subjective symptoms outside of menstruation. Exclusion criteria of this trial were undiagnosed genital bleeding and/or abnormal findings on gynecological exam other than endometriosis, use of hormonal therapy for endometriosis within 16 weeks before enrollment, pregnancy, lactation, desire to conceive during treatment, previously failed treatment of endometriosis using the medications involved in the study, history of severe drug reaction or hypersensitivity to steroid hormones, contraindications to combined oral contraceptives outline by World Health Organization and Centers for Disease Control and Prevention, and finally a prior surgical treatment or exam for endometriosis within a menstrual cycle before the start of medication.

After eligibility was determined, the women were randomized in a 1:1 ratio using a computer-generated sequence. They either received 2 mg/day dienogest or a COC (Yasmin, 0.03 mg ethinyl estradiol and 3 mg drospirenone) for 24 weeks. The population size of each group was 35. Participants followed up at weeks 12 and 24 after initiating treatment for evaluation of medication efficacy through a variety of subjective surveys. The primary efficacy variable of this

trial was absolute change in endometriosis-associated pelvic pain from baseline to post-treatment, which was assessed using the visual analog scale (VAS). The second efficacy variable was the change in the Biberoglu and Behrman (B&B) scale for pain symptoms. Health related quality of life was assessed using the Endometriosis Health Profile-30 (EHP-30) questionnaire. In between the follow up visits, participants were also instructed to keep a pain score diary tracking their symptoms, pain levels, and analgesic use.

Both treatment groups had comparable baseline characteristics within each category. By the end of the trial at week 24, the VAS score decreased significantly for both groups. The scores for the women taking dienogest decreased from 8.40 ± 1.3 to 2.44 ± 2.1 ($p < 0.0001$). In the group of women taking the COC, their VAS score decreased from 7.92 ± 1.5 to 3.38 ± 3.1 ($p < 0.0001$). By the end of the treatment, there was also a significant improvement in the number of women reporting moderate to severe in regards to dysmenorrhea, dyspareunia, and pelvic pain. By week 24, those who reported none or mild severity in the dienogest and COC groups respectively were 80% vs 73.1% for dysmenorrhea, 75% vs 58.3% for dyspareunia, and 80% vs 88.5% for pelvic pain. Health-related quality of life also improved for both groups but was not statistically significant. Adverse effects, such as abnormal uterine bleeding, mood swings, headache, nausea, and breast pain/tenderness were more common within the group taking COCs, but the dienogest group experienced these as well.

Overall, this study found dienogest to be as effective as the combined oral contraceptive, Yasmin, in relieving endometriosis-associated non-cyclical pelvic pain, dysmenorrhea, dyspareunia, and health-related quality of life. There were various strengths identified in this study, which included the randomized controlled design, the use of multiple evaluations to measure the efficacy, extensive inclusion and exclusion criteria, and the similar population

demographics within each group. Areas identified as the trial's weaknesses were the short duration, no control group, the allowed use of analgesics throughout the trial, and the use of only subjective scales to evaluate effectiveness of treatment (El Taha et al., 2021).

Harada and Momoeda (2016) conducted a placebo-controlled, double-blind, randomized trial evaluating the efficacy and safety of an ultra-low-dose oral contraceptive in subjects with dysmenorrhea. The populations used included two hundred fifteen subjects with dysmenorrhea and was conducted at 18 different centers in Japan. The inclusion criteria required the patient be at least 16 years of age, have regular menstrual cycles (28 ± 2 days), have primary or secondary dysmenorrhea diagnosed, and have the presence of moderate to severe dysmenorrhea based on a total dysmenorrhea score of 3-6. The exclusion criteria were having a history of treatment, medical or surgical for dysmenorrhea within 8 weeks of entry to the study, or use of medication that affect the metabolism of oral contraceptives.

The participants were randomly assigned to receive 0.02 mg ethinyl estradiol and 1 mg norethisterone (NPC-01), placebo, or 0.035 mg ethinyl estradiol and 1 mg norethisterone (IKH-01) for four cycles. Subjects with primary dysmenorrhea were randomized at a 2:1 ratio for treatment of NPC-01 (n = 55) or placebo (n = 28). The initial dysmenorrhea score for patients with primary dysmenorrhea in the NPC-01 group was 3.9 (0.92) and placebo group was 4.3 (0.90). The subjects with secondary dysmenorrhea were randomized at a ratio of 2:1:2 to receive NPC-01 (n = 50), placebo (n = 26), or IKH,01 (n = 47). The initial dysmenorrhea score for the subjects with secondary dysmenorrhea in the NPC-01 group was 4.3 (1.05), the placebo group 4.1 (0.99), and the IKH-01 group was 4.0 (0.87). The mean age of NPC-01 was 32.4 (SD of 7.29), placebo was 30.4 (7.41), and IKH-01 was 34.0 (6.93).

To evaluate the efficacy of these interventions, a total dysmenorrhea score (verbal pain scale) was used to assess pain in terms of limited ability to work and need for analgesics. Reductions in total dysmenorrhea score were significantly higher in the NPC-01 group (-2.3) than the placebo group (-1.3) ($p < 0.001$). This was similar in efficacy to the IKH-01 group. Side effects were found to be significantly higher in the NPC-01 group than the placebo group (89.7% vs. 57.4%).

Overall, this study concluded that ultra-low-dose contraceptive NPC-01 is as effective as IKH-01 in treatment of dysmenorrhea relief. One of the strengths of this study was that it was a placebo-controlled, double-blind study. It also had a large N group, which included subjects that had either primary or secondary dysmenorrhea, which helps to evaluate the effectiveness of treatment on both populations. Weaknesses of this study include the uneven number of subjects within each group, the lack of diversity in subjects, and the involvement of a pharmaceutical company, which could indicate bias (Harada & Momoeda, 2016).

Osuga et al. (2020) conducted a 52-week open-label, multicenter, long-term treatment study evaluating the safety and efficacy of dienogest (DNG), an oral progestin pill, in subjects with primary and secondary dysmenorrhea. The population of the study included 147 Japanese patients and took place at 17 different institutions in Japan. The patients needed to be aged 20 years or older, have regular menstrual cycles of 38 days or less, have either primary or secondary dysmenorrhea that was diagnosed by ultrasonography and pelvic exam, and they needed to have a dysmenorrhea score of at least 3. There were 74 subjects with primary dysmenorrhea and 73 with secondary. Exclusion criteria for this study were patients with primary dysmenorrhea that have a history of endometriosis, adenomyosis, uterine myoma, or secondary dysmenorrhea; patients with secondary dysmenorrhea with a history of submucous leiomyoma; any patient who

could not distinguish their lower abdominal pain from back pain due to dysmenorrhea; any patient with uterine enlargement with a maximum diameter of 100.0 mm or maximum thickness of the myometrium of 40.0 mm; and any patient that has a history of or currently has severe anemia with a hemoglobin lower than 8.0 g/dL.

Patients received 1 mg of DNG orally each day for 52 weeks, but at or after 12 weeks the patients could increase the dose to 2 mg orally each day if they were not experiencing relief in dysmenorrhea symptoms. Only 16 out of 147 patients increased their dose of DNG. Multiple endpoints were evaluated during this study. The primary safety endpoint evaluated adverse effects, while the secondary endpoint evaluated adverse drug reactions. Patients were instructed to keep a diary of symptoms to record the number of days and severity of genital bleeding throughout the study. This study also utilized the dysmenorrhea score to evaluate lower abdominal pain and lower back pain.

The results indicated a change in dysmenorrhea score from baseline (mean ± standard deviation) of -3.7 ± 1.6 at week 24 and -4.0 ± 1.3 at week 52. The response rate based on the dysmenorrhea score was 73.7% by week 52. Genital bleeding was more common in those with secondary dysmenorrhea than primary. There were numerous adverse events noted, with the most frequent being irregular uterine bleeding (94.6%). Other less frequent symptoms noted include malaise, menorrhagia, breast discomfort, and headaches. The bodily pain score was 37.5 ± 17.8 at baseline and at week 52 of treatment improved to 81.7 ± 20.8. This suggests that DNG treatment contributed to an improved quality of life.

Overall, this study indicates favorable outcomes regarding dysmenorrhea and pain relief for those who use DNG long-term. One main strength of this study is that includes patients with both primary and secondary dysmenorrhea. It also had a lengthy selection process and excluded

many populations that could change the results due to other conditions. This study had a few different weaknesses including the small population size and a lack of a control group, which would have helped strengthen their findings. A potential bias of this study is that it was funded by a pharmaceutical company and could therefore have bias towards their own oral contraceptive (Osuga et al., 2020).

Petraglia et al. (2014) conducted a double-blind, double-dummy, parallel-group study comparing estradiol valerate plus dienogest (E2V/DNG) versus ethinylestradiol plus levonorgestrel (EE/LNG) in reducing the number of days with dysmenorrhea pain in women with primary dysmenorrhea. The population studied included otherwise healthy women between the ages of 14 to 50 years who were requesting contraception and had a diagnosis of primary dysmenorrhea. Exclusion criteria for this study were pregnant or breastfeeding women, women with a BMI of more than 32, and women with pelvic pathology. After determining the women were eligible, they were then randomized to treatment using a computer-generated randomization list. 253 women were placed into the E_2V/DNG plus placebo group and 230 women were placed into the EE/LNG plus placebo group for three cycles lasting 28 days each.

To assess treatment compliance and treatment efficacy, women kept diary cards to document treatment, symptoms, pain severity and use of analgesics. The primary efficacy variable studied was the number of days women endured dysmenorrhea pain. The second efficacy variable studied was the total points scored for dysmenorrhea pain, number of days with pelvic pain independent of vaginal bleeding, analgesic use, interference of pain on work, school or other activities, bleeding patterns, and amount of sick leave taken. Questionnaires used to evaluate the treatment efficacy included the Resource Use Questionnaire, the General Health and

Well-Being Questionnaire Short Form 36 version 1, and the Global Clinical Impression. These were completed before, during and after the end of the study.

Overall, for both the primary and secondary efficacy variables, there were similar changes from baseline for each group. The change from baseline for number of days with dysmenorrhea pain was -4.6 ± 4.6 days in the E_2V/DNG and -4.2 ± 4.2 days for the EE/LNG group (mean ± SD). Total dysmenorrhea pain for the E2V/DNG and EE/LNG was -10.6 ± 9.7 vs -10.0 ± 8.9 (p=0.34). This indicates that the results were not significant enough to show superiority of E2V/DNG. The mean change in days with pelvic pain in the absence of vaginal bleeding was -4.0 ± 5.7 (E_2V/DNG) vs -3.7 ± 5.7 (EE/LNG). Finally, the mean change for number of tablets consumed of ibuprofen was -6.2 ± 14.8 (E_2V/DNG) vs -6.6 ± 12.3 (EE/LNG).

The results indicate that both treatments provided improvement of dysmenorrhea complaints in women with primary dysmenorrhea. The treatment decreased the number of days of dysmenorrhea pain, reduced the number of points for dysmenorrhea pain, decreased the number of days spent with pelvic pain independent of vaginal bleeding, and decreased analgesic use. One of the major limitations of this study was the short duration. Another limitation was the use of a 4-point scale for evaluation of pain instead of using a validated questionnaire or visual analog scale. Strengths of this study include utilizing only females with primary dysmenorrhea, having a variety of demographics for the population, and having a larger sample size (Petraglia et al., 2014).

Patient quality of life with use of oral contraceptives for dysmenorrhea

Priya et al. (2016) conducted an open-label, randomized prospective interventional study comparing the use of combined hormonal vaginal ring (CVR) and low dose combined oral hormonal pills (CHP) in women with chronic pelvic pain. The duration of the study was 18

months and involved 60 women, 30 within each study group. Sexually active women who were aged between 18 and 45 years old, who also had a history of pelvic pain for more than 6 months were included in the study. Exclusion criteria for these women were women with gynecological conditions (endometriosis, adenomyosis, fibroids, ovarian remnant syndrome, chronic PID, cervical stenosis), gastrointestinal disorders, urinary problems, musculoskeletal disorders, neurological diseases, and women with psychosocial issues such as depression. Once women met the inclusion criteria and were selected to participate, they were randomized into two groups, CVR (study group) and CHP (control group), using a computer-generated system.

The women then received either the CVR or CHP for 84 days. The ring was comprised of 15 mcg ethinyl estradiol and 120 mcg etonogestrel. The oral pill consisted of 30 mcg ethinyl estradiol and 150 mcg levonorgestrel. Participants were evaluated initially for a baseline, then at the end of the first, second, third, and fourth month. The four month follow up was the last and it took place a month after the treatment was completed. The primary outcome measured relief of pain by using the visual analog scale (VAS) and the verbal rating scale (VRS). The secondary outcomes being measured were satisfaction of method, compliance, user acceptability, change in frequency of sexual intercourse per week, and complications. These were assessed at every follow-up.

The VAS score at baseline for CVR was 8.23 ± 0.62 and for CHP was 7.93 ± 0.78. Scores improved at each follow up and by the end of the fourth month, the CVR group was 3.77 ± 2.56 and the CHP group was 4.03 ± 2.33. The VRS scores also showed improvement for both groups. The CVR group started at 7.23 ± 2.01 and ended at 2.73 ± 2.03. The CHP group started at 6.23 ± 2.20 and ended at 3.37 ± 2.21. The VAS and VRS scores had decreased for both the CVR and CHP groups, but the p value estimating the significance between the two groups was 0.599,

which means it was not significant. Dysmenorrhea improved significantly for each group, CVR from a median of 2.5 to a median of 1, CHP from a median of 2 to 1 ($p < 0.001$). Noncyclic pelvic pain also significantly improved from a median score of 3 to 1 for CVR and 3 to 2 for CHP ($p < 0.005$). Finally, deep dyspareunia also improved significantly for each group from 3 for CVR and 2 for CHP to 0 for both groups ($p < 0.005$).

Compliance, satisfaction, and accessibility were also found to be higher in the CVR group versus the CHP group but was not statistically significant ($p = 0.371$). Side effects that were noted to be higher in the pill group were nausea, headache, and bloating. All women did experience amenorrhea initially with treatment, but most resumed their menses within 10 days from the start of treatment.

This study concluded that the combined hormonal vaginal ring was comparable in efficacy to the oral hormonal pill for treating women with idiopathic chronic pelvic pain. Some strengths of this study were the diverse group of women chosen to participate and the lengthy exclusion criteria, making it more directed towards primary dysmenorrhea. Weaknesses of the study were the small sample size, not having a control group with solely placebo, and having the study open label (Priya et al., 2016).

Sukhikh et al. (2021) conducted a prospective, open-label, multicenter observational study comparing the efficacy of two different dydrogesterone regimens for treatment of endometriosis with chronic pelvic pain. There were 350 women chosen for this study. They were between the ages of 18 to 45 years old, had a diagnosis of endometriosis with chronic pelvic pain, with or without dysmenorrhea, and met extensive inclusion criteria. These criteria include having a laparoscopic confirmed diagnosis of endometriosis in the lower abdominal area, a transvaginal pelvic ultrasound for ovarian cyst detection performed prior to two months before study

inclusion, having been prescribed dydrogesterone, and no hormonal treatment for at least two cycles prior to enrollment into the study. There were also extensive exclusion criteria such as any disease or genital disorder requiring continuous medical treatment, regular use of analgesics for anything but to relieve endometriosis associated pain, use of hormonal contraception during the previous two cycles, pregnancy, menopause of premature ovarian insufficiency, having a contraindication to the treatment, abnormal cervical cytology test, and treatment for infertility by reproductive technologies.

Participants were placed into their respective groups based off of what medication their prescribing physician had started them on. There were 273 patients placed in the prolonged cyclical treatment which was 10 mg of dydrogesterone 2-3 times daily between the 5^{th} and 25^{th} days of their menstrual cycle. A total of 77 women were placed in the continuous regimen of dydrogesterone. The data cutoff for the two groups was at six months. The primary endpoint of the study was changes in intensity of chronic pelvic pain, which was measured with the 11-point numerical rating scale (NRS). The secondary endpoints were number of days of analgesics use per menstrual cycle, severity of dysmenorrhea, duration of menstrual cycles, patient-reported sexual well-being, and health related quality of life. Analgesic use was measured by patient diary. Severity of dysmenorrhea was measured using the 11-point NRS. The patient's sexual well-being was reported using the 5-point Likert scale. Lastly, the quality of life was measured using the Short Form-20 (SF-20).

These patients were evaluated a total of 3 times, at baseline, after three months, and after six months. At the end of treatment, the change from baseline improved significantly for chronic pelvic pain intensity and was -3.3 ± 2.2 ($p < 0.0001$) for patients receiving the prolonged treatment and -3.0 ± 2.2 ($p < 0.0001$) for patients receiving continuous treatment. Although

statistically significant in regard to improvement, it was not statistically significant between the two groups. Participants in both groups also experienced a reduction in the amount of days analgesics were used and the severity of dysmenorrhea. They also experienced no change in duration of menses, an improvement in sexual well-being, and an increase in healthy related quality of life. Once again, there was no significant difference between the two treatment groups. The most common side effect the women experiences was uterine bleeding, which was only reported in the group receiving continuous treatment.

This study determined that there was similar efficacy between the prolonged group and continuous group in improving quality of life and sexual well-being, and reducing chronic pelvic pain, analgesic use, and dysmenorrhea severity in women with endometriosis. There were some noted limitations of the study such as absence of randomization, short duration of study, and bias treatment selection. Strengths of this study may include the large overall population size, the diversity of the population, and the extensive inclusion/exclusion criteria (Sukhikh et al., 2021).

Effectiveness of intrauterine devices for dysmenorrhea

Maguire et al. (2015) conducted a planned secondary analysis of a randomized, double-blind, placebo-controlled study evaluating the use of intracervical lidocaine gel during intrauterine device (IUD) insertion. The initial study randomized the women to the lidocaine gel group or placebo group, which was determined to not influence insertion pain and was unrelated to IUD removal. The secondary analysis primarily focused on detecting early predictors for early discontinuation of IUDs by comparing baseline characteristics, such as dysmenorrhea. The women who participated in this study were English or Spanish speaking, aged 18-45 years old, and were wanting an IUD for birth control. The only exclusion criteria was women who were

pregnant within the past month. There were 199 women included in the trial and they were able to choose whether they wanted to receive the Levonorgestrel-releasing intrauterine system (LNG-IUS) or the copper T380A intrauterine device (Cu T380A). A total of 62 women chose LNG-IUS and 137 chose Cu T380A.

Baseline questionnaires were given to the participants which included the visual analog scale (VAS) to rate dysmenorrhea pain. Women used this scale to rate pain before, during each step of the insertion, and throughout the year. Baseline dysmenorrhea was noted to be similar between the two groups and was not statistically significant ($p = 0.18$). The participants were tracked through and EMR system to track IUD removals. Within the first year of the study, there were 21 IUD removals and 7 expulsions found. The research notes that of the removals, six women who chose the LNG-IUS had a statistically significant higher baseline dysmenorrhea ($p = 0.03$) than the 15 removals in the Cu T380A group. Baseline dysmenorrhea pain was higher overall in the women who chose IUD removal versus continuation, which was statistically significant as well (42 vs. 25.5, $p = 0.03$). The original randomized trial found dysmenorrhea to be a predictor of higher IUD insertion pain. The secondary analysis given of this study indicates that a higher baseline dysmenorrhea was associated with IUD removal within 1 year. Some limitations of this original study and study analysis include having a small number of removals which did not allow for more predictors of IUD removal and the use of only one EMR causing the information to potentially be inaccurate due to not knowing if females had their IUDs removed elsewhere. Some strengths of these studies include a large population size, the duration of the study, and using a secondary analysis that focused primarily on dysmenorrhea pain predicting IUD tolerance (Maguire et al., 2015).

Shaaban et al. (2015) conducted a clinically registered open, parallel, randomized controlled trial that compared the effectiveness of the levonorgestrel releasing intrauterine system (LNG-IUS), Mirena, with the low dose combined oral contraceptive (COC), Gynera, in treating adenomyosis related pain with or without uterine bleeding. Women who presented to a specific clinic and had complaints of pelvic pain, either dysmenorrhea or chronic pelvic pain, were entered into a screening phase. A total of 62 women were selected to participate after they were determined to be eligible. To be included in the study the women had to have requested contraceptives for at least 6 months, be aged 20-45 years old, be a resident near the clinic, and be willing to accept either type of treatment. Women were excluded from the study if they had a history of ectopic pregnancy, puerperal sepsis, pelvic inflammatory disease, evidence of coagulopathy, abnormalities of the uterine cavity, had a history of malignancy of histological evidence of endometrial hyperplasia, adnexal abnormalities, undiagnosed vaginal bleeding, or if they had any contraindications to COCs. The 62 women chosen were randomized using a computer-generated random table which placed them into either the LNG-IUS group or the COC group, 31 per group.

The COC Gynera consisted of 30 mcg of ethinyl estradiol and 75 mcg of gestodene. The primary endpoint of this study was measuring pelvic pain, dysmenorrhea or chronic pelvic pain, with the visual analog scale (VAS). The secondary endpoints were the measure of the menstrual blood loss using a patient diary, and both uterine arteries and intramyometrial blood flow was measured by Doppler ultrasound. They were then reassessed after the first, third, and sixth month. At the end of the study, participants were also asked to rate their overall satisfaction with their treatment.

VAS scores for pelvic pain decreased significantly in each group by the end of treatment ($p < 0.001$). The Mirena group had a larger reduction in pelvic pain compared to the Gynera group, 6.23 ± 0.67 to 1.68 ± 1.25 vs. 6.55 ± 0.68 to 3.90 ± 0.54, respectfully. The number of days bleeding, amount of blood lost, and uterine volume were also more significantly reduced in the Mirena group ($p < 0.001$). The doppler results indicated the blood vessels being measured increased significantly from baseline, more in the LNG-IUS group versus COC group ($p <0.000$). There was also a greater percent of participants satisfied with their treatment in the Mirena group.

This study determined that both LNG-IUS and COCs are effective in reducing pain and bleeding associated with adenomyosis. However, LNG-IUS was shown to be superior in relief of symptoms. One limitation noted was that the transvaginal ultrasound and color Doppler ultrasound only had a specificity of 86% and 86.67% respectively. Other limitations include the inability to make the participants blind to the type of treatment they were receiving and the small sample size. Strengths of this study include randomizing the participants, using both qualitative and quantitative measures, and using extensive inclusion and exclusion criteria to narrow the study population (Shaaban, et al., 2015).

Teal et al. (2019) conducted a comprehensive contraceptive efficacy and safety study to assess the levonorgestrel 52 mg intrauterine system (LNG 52-mg IUS), Liletta. The data from this study was taken from the first 5 years of a 10-year phase 3 contraceptive trial. Out of the 1,751 women enrolled in the study, only a total of 1,714 participants underwent a successful IUS placement. A total of 30 women were lost to follow up and others were excluded from the data due to desiring pregnancy, withdrawing consent, or discontinuing due to adverse effects. This left 1,538 participants to be included in the data. Only 495 women made it the 5-year mark, and 176

to the 7-year mark for the same reasons previously listed. The women included within the study had to be healthy, sexually active (at least four times per month) and have a regular menstrual cycle (21-35 days). Exclusion criteria was given to ensure patients were of good health, potential fertility, and have a low risk for adverse effects.

The women were instructed to follow up at months 1, 3, 6, and 12 in the first year. Then after the first year, they were instructed to follow up every 6 months. At these follow ups, string placement would be confirmed, and patient's symptoms would be evaluated. In between visits, patients had to keep a diary documenting all the symptoms they experienced, amount of bleeding experienced, and other contraceptives used. The primary efficacy outcome was studying pregnancy rate on this treatment. These rates were calculated using the Pearl Index.

At the end of the 5 years, the 5-year life pregnancy rate was only 0.92%, which equates to 14 pregnancies throughout that time frame. Amenorrhea rates also increased with about half of the patients experiencing this within the first year. An improvement in menstrual cramping was also reported. Women who reported severe cramping at baseline, 41.9%, 48.1%, and 47.7% reported none at years 1,2, and 3, respectfully. Dysmenorrhea was an adverse effect reported in a total of 107 women, which was statistically significant ($p = 0.02$). Overall, this study showed that LNG 52-mg IUS was effective for contraception purposes over the five-year period. It also had a low discontinuation rate for adverse effects. It was noted that younger females were significantly more likely to report new or worsening acne, dysmenorrhea, dyspareunia, and pelvic pain, while older women were more likely to report weight increase with this treatment option. There was a total of 322 participants who discontinued the IUS due to adverse effects previously listed. Major strengths of this study were the population size and the duration of trial. Limitations of this trial

include being funded by a pharmaceutical company, not having a control group, and having few assessment tools (Teal et al., 2019).

Patient quality of life with use of intrauterine devices for dysmenorrhea

Carvalho et al. (2018) conducted an open-label, parallel-group, noninferiority randomized clinical trial comparing the efficacy of etonogestrel (ENG)-releasing contraceptive implant with the 52-mg levonorgestrel-releasing intrauterine system (LNG-IUS) in treating pelvic pain associated with endometriosis. A total of 103 women were included within this trial. Inclusion criteria was having a diagnosis of stage 1-IV endometriosis, complaints of noncyclic chronic pelvic pain and dysmenorrhea for more than 6 months, be clinically healthy, not pregnant, aged 18-45, able to follow up, willing to be randomized to treatment. Exclusion criteria were women who had surgical or hormonal treatment for endometriosis within 2 months of enrollment. After women were determined to be eligible, they were randomized to receive either the ENG implant (n= 52) or LNG-IUS (n=51), using a computer-generated program.

Participants were evaluated using a variety of questionnaires and methods at baseline, 1 month after insertion and at 6 months of treatment. The primary outcome of this trial was the change in endometriosis-associated noncyclic pelvic pain and dysmenorrhea. The secondary outcome evaluated the changes in health-related quality of life. Bleeding patterns, daily symptoms, amount of pain were recorded into a patient diary. Their pain was evaluated using the visual analog scale (VAS). Health related quality of life (HRQoL) was evaluated using the Endometriosis Health Profile-30 (EHP-30) questionnaire.

VAS scores did not significantly differ between the two groups ($p = 0.241$ and $p = 0.431$ respectfully). Both groups did have a significant decrease in noncyclic pelvic pain, ENG from 7.6 ± 1.7 to 5.6 ± 1.7 and LNG-IUS from 7.4 ± 1.7 to 1.9 ± 1.7 ($p < 0.0001$). VAS scores for

dysmenorrhea also decreased significantly in both groups, ENG from 7.5 ± 1.7 to 2.2 ± 3.2 and LNG-IUS from 7.3 ± 1.7 to 1.9 ± 2.2 ($p < 0.0001$). The HRQoL also showed significant improvement in both groups in all aspects of quality of life ($p < 0.05$), except for the portion evaluating possibility of conceiving, which was not statistically significant.

The findings in this trial indicate that the ENG implant and the 52-mg LNG-IUS are similarly effective in relieving endometriosis-associated noncyclic pelvic pain and dysmenorrhea, and in the improvement of the participants health related quality of life. The strengths identified were the randomized clinical trial design and having similar stages of endometriosis among most participants. Limitations identified were losing 10% of patients to follow up, the short duration of the trial, not being able to blind the participants to treatment, and not having a control/placebo group (Carvalho et al., 2018).

Ekin et al. (2013) conducted a pilot study evaluating the treatment of adenomyosis with the levonorgestrel-releasing intrauterine system (LNG-IUS) to improve urinary incontinence, irritative and obstructive symptoms to improve a patient's quality of life. There was a total of 65 women who participated in the study. In order to be selected for the study, women had to have been experiencing heavy prolonged menstrual bleeding with dysmenorrhea for over 3 months, have a diagnosis of adenomyosis on ultrasound, desire LNG-IUS for contraception, have no contraindications to the treatment, and be willing and able to follow up after treatment. Women excluded from the study were those with pre-existing neurological diseases, diabetes, arterial hypertension, thyroid dysfunction, and symptomatic pelvic organ prolapse.

The participants followed up at month one and six after insertion. They were given two questionnaires at baseline and at their follow ups to evaluate treatment efficacy. The Urogenital Distress Inventory (UDI-6) screened for stress, irritative and obstructive symptoms. The

Incontinence Impact Questionnaire (IIQ) evaluated how these symptoms affect the participants' quality of life with regard to physical activity, travel, social relations, and emotional health.

There was an overall significant improvement in total UDI scores, 3.49 ± 3.55 from the baseline of 5.43 ± 4.59 ($p < 0.0001$), after the six months of treatment. It was also noted that the improvement of UDI scores were significantly correlated with improvements of menorrhagia and dysmenorrhea. Total IIQ scores were found to be significantly lower at the six month follow up 1.22 ± 2.48 from baseline of 3.18 ± 4.98 ($p < 0.0001$).

The results of this study indicate that LNG-IUS is an effective treatment in menorrhagia, dysmenorrhea, and urinary incontinence with irritative and obstructive symptoms in patients with adenomyosis, thus improving those participants' quality of life. Limitations identified within this study were the small sample size, short duration, using only ultrasound to diagnose adenomyosis, and not having a control/placebo group. Strengths of this study include using validated questionnaires and having extensive inclusion and exclusion criteria (Ekin et al., 2013).

Discussion

Although there are minimal studies that research treatment of dysmenorrhea and even less that compare treatments for dysmenorrhea, the cumulative data shows that using either combined oral contraceptives or intrauterine devices are effective options. Currently, the most common treatment recommended for patients with dysmenorrhea are NSAIDs. This may work well for some, but may not work well or can be contraindicated for others. Long term NSAID use can also have detrimental side effects on various organ systems, such as gastrointestinal, cardiovascular, hepatic, and renal. People who are unable to take NSAIDs need alternative

treatment options to help improve their quality of life by decreasing the amount of pain they experience with their menstrual cycles.

There are a handful of studies that evaluate or compare different types of oral contraceptives in the effectiveness of treating dysmenorrhea. There are many kinds of oral contraceptives. Some contain progestin only, while others are combined with both progestin and estrogen, and many of them come in different doses. Each one of these studies indicates that oral contraceptives work well individually, or in addition to NSAID use. The studies included within the literature review evaluated both combined oral contraceptives and progestin only contraceptives and found that each were effective options in treatment of both primary and secondary dysmenorrhea. Majority of the women evaluated experienced decreased levels of pain associated with their menses. The oral contraceptives were also often associated with long-term use due to their effectiveness but were noted to have a variety of side effects with use. The most common side effects experienced were infrequent or irregular uterine bleeding. However, most patients preferred to continue use and endure the side effects since it reduced the amount of pain associated with their menses.

The studies included in the literature review that evaluated intrauterine devices determined that they were safe and effective options in treatment of menstrual pain. The IUDs were typically well-tolerated by patients and the majority reported decreased analgesic use. However, there was a higher likelihood of side effects that resulted in some of the patients discontinuing the treatment. Some of the side effects most noteworthy were amenorrhea, worsening dysmenorrhea, dyspareunia, or expulsion of the IUD. There are different types of intrauterine devices, but the only ones included within this literature review were levonorgestrel releasing IUDs. Therefore, this literature review cannot conclude whether copper intrauterine devices have a similar effect.

Out of all the studies included within the literature review, only one (Shaaban, et al., 2015) compared an intrauterine device with combined oral contraceptives. This proved to be most useful in evaluating the question of which treatment type is more effective at treating dysmenorrhea. The study focused on pain associated with secondary dysmenorrhea, or more specifically, patients with adenomyosis, but is still applicable to the research question identified in this paper. It was determined that although both oral contraceptives and intrauterine devices were effective in decreasing menstrual pain, the intrauterine device was superior to the oral contraceptive in decreasing pain. Although not entirely supported by evidence, it could be speculated that oral contraceptives are not as effective due to inconsistency of times the medication was taken, differences in absorption rates in women, or various other reasons.

Conclusion

The data within this literature review verifies that both oral contraceptives and intrauterine devices are safe and effective options in reducing dysmenorrhea pain. The data of the one study that compared the two different treatment options showed that intrauterine devices are superior to oral contraceptives for treatment of dysmenorrhea. However, there needs to be more studies comparing the two. There are also many different types of oral contraceptives and intrauterine devices that should be studied and compared. There was a high prevalence of side effects noted for both treatment populations. Some patients may tolerate oral contraceptives better than the intrauterine device, while others may prefer the intrauterine device to the oral contraceptives. Until there is further research, the data will continue to indicate that intrauterine devices are superior in the treatment of dysmenorrhea.

To have a more precise answer to the question of which treatment is more effective in pain control for dysmenorrhea, there needs to be more studies completed. The studies should be

more exclusive. This means that they should study primary dysmenorrhea versus secondary. They should also have narrowed criteria for trial entry by limiting age ranges, parity, other comorbidities, or anatomical abnormalities. To truly know if oral contraceptives or intrauterine devices are better at pain control, the studies should focus on comparing the two treatment options. Only then will there be a better understanding of the treatment options.

Applicability to Clinical Practice

The data from this literature review should provide medical professionals with a guide in their clinical practice to aid in potentially better treatment of patients with dysmenorrhea through clinical-based evidence. Providers will be able to help suggest treatment options, such as combined oral contraceptives or progestin-only intrauterine devices, that may be better tolerated and more effective for their patients based on this data. They will also be able to better understand the effect dysmenorrhea has on the lives of each and every patient. Dysmenorrhea has a severe impact on the quality of life of women and will start to be taken more seriously as more research is conducted and more providers are educated on the matter.

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