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MANAGEMENT OF UTERINE FIBROIDS: AN INTEGRATIVE APPROACH

A CAPSTONE PROJECT
SUBMITTED TO THE GRADUATE FACULTY
OF THE GRADUATE SCHOOL
BETHEL UNIVERSITY

BY

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IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
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MASTER OF SCIENCE IN NURSING

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Management of Uterine Fibroids: An Integrative Approach

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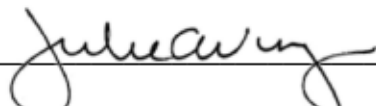
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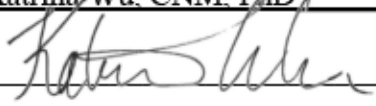
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Abstract

Introduction: Uterine fibroids (UF) affect at least 1 in 4 adult women and are the most frequent type of tumor affecting the female reproductive organs of women of reproductive age. This integrative review will examine alternative methods used to manage symptomatic uterine fibroids to determine if they could be effective alternatives to invasive procedures.

Methods: The official methodology was conducted using the CINAHL, PubMed, and Scopus databases to identify relevant original research for inclusion. Articles were included if they were original research studies published between 2002-2023, written in English, and discussed integrative options for preventing and treating uterine fibroids. Citation searching served as a secondary search method. A matrix was completed, and quality was analyzed using the Johns Hopkins Appraisal Tool.

Results: This integrative review includes eight studies on Traditional Chinese Medicine, two on lifestyle modification, and eight on supplementation. Daily supplementation with vitamin D, vitamin B6, and ECGC demonstrated a significant decrease in the volume and symptoms of uterine fibroids, improved anemia, and had positive effects on quality of life. This research found that Traditional Chinese Medicine was associated with a decrease in uterine fibroid-related symptoms, decreased risk of developing fibroids, and a reduction in fibroid size and volume. A sample size of 21 studies was concluded in this research.

Discussions: The studies identified in this integrative review consistently demonstrated the potential positive impact integrative therapies of various modalities can have on uterine fibroid

management with minimal to no risks. The overall recommendation is that additional, well-designed clinical trials with larger sample sizes and of higher quality be undertaken.

Keywords: uterine fibroids, leiomyoma, herbs, alternative medicine, complementary medicine, integrative medicine

Management of Uterine Fibroids: An Integrative Approach

Introduction

Uterine Fibroids are the most common type of benign pelvic tumor (Mirello et al., 2021). They affect at least 1 in 4 adult women of reproductive age (Harris et al., 2022). Uterine fibroids affect up to 70% of Caucasian women and more than 80% of Black women, with Black women reporting higher prevalence, symptom intensity, and overall disease burden (Al-Hendy et al., 2017; Riggan et al., 2021). Between 25% and 50% of women with fibroids have symptoms, including heavy periods, infertility, uterine pain, increased frequency of urination, and anemia. (Marsh et al., 2018).

The symptoms experienced by women who suffer from uterine fibroids can grossly impact their quality of life. Ghant and Sengoba et al. (2015) carried out research that qualitatively evaluated the impact of uterine fibroids on women's emotional and mental health. The findings showed that the majority of subjects experienced strong emotional reactions to their fibroids, which included worry, fear, rage, and depression. Among these women, 50% felt helpless and came to believe they had little to no power to control their fibroid diagnosis and were not given non-surgical management options. Additionally, several women felt they lacked significant support to assist them in coping with the various challenges.

Fibroids can be managed with surgical interventions like a myomectomy to remove the fibroids or a hysterectomy to remove the uterus (Liu et al., 2013). In the United States, fibroids are the number one indication for hysterectomies and are the primary reason for gynecologic hospitalizations unrelated to pregnancy (Harris et al., 2022). Hysterectomies present risks, which include early ovarian failure and menopause, depression, the need for additional surgery, and other sequelae which may be exacerbated by hysterectomies (Madueke-Laveaux et al., 2021). A

qualitative study conducted by Riggan et al. (2021) examined 47 women's experiences and perceptions of the diagnosis and management of uterine fibroids. Participants in the study expressed shock when doctors recommended surgery as the first or only course of therapy, especially hysterectomy. Many felt they were being forced to choose from a limited range of options that were not in line with their treatment and fertility goals. Unfortunately, the American College of Obstetricians and Gynecologists and the American College of Nurse-Midwives do not have professional statements that endorse the use of integrative methods as an effective and safe alternative or complementary management strategy for uterine fibroids. Perhaps this will change as research continues to develop in this specialty area.

Imogene King's theory of goal attainment explains the interpersonal relationship between a provider and client, the shared decision-making process, and the actions performed to achieve patient-centered goals. King has developed three fundamental needs within this theory: (1) the need for health information; (2) the need for care that seeks to prevent illness; and (3) the need for care when unable to help oneself. Complementary therapy has the potential to reduce the severity of symptoms and potentially decrease the need for invasive interventions for fibroids among women. In a study by Jacob et al. (2014), 38-46% of the participants reported that their symptoms were "a lot better" after receiving complementary and alternative medicine (CAM) therapies for their fibroid-related symptoms. King's approach emphasizes the value of clients' involvement in fully informed decision-making. It places equal emphasis on both the interaction between nurses and clients and the results of the care clients receive. According to Riggan et al. (2021), increased patient participation and autonomy in the management of uterine fibroid may be facilitated by efforts to actively involve women in the shared decision-making process, along

with providing alternatives to nonsurgical therapies. These efforts may also enhance treatment acceptance.

This integrative review will examine the efficacy of different integrative methods used to manage symptomatic uterine fibroids. These methods may support the use of integrative therapy as an effective alternative treatment option to invasive procedures like hysterectomies or myomectomies. These non-invasive, integrative methods can be employed by Advance Practice Registered Nurse (APRNs) as treatment and prevention recommendations for patients who desire a holistic approach for fibroid management.

Methods

This review followed the standards for performing an integrative review presented by Whittemore and Knafl (2005). This framework includes five stages: problem identification, literature search, data evaluation, data analysis, and presentation.

On January 18, 2023, an initial search in CINAHL, PubMed, and Scopus was conducted to identify relevant articles for inclusion, using the following search terms with Boolean operators: uterine fibroids, leiomyoma, herbs, alternative medicine, complementary medicine, complementary therapies, integrative medicine, lifestyle changes, traditional medicine, Chinese traditional medicine, functional medicine, naturopathic medicine, and ayurvedic medicine. Articles were included if they were original research studies published between 2002-2023, written in English, and studied integrative options for the treatment and prevention of uterine fibroids. Articles were excluded if they solely addressed the medical and/or surgical management of uterine fibroids. The initial electronic database search produced a total of 198 publications, which were uploaded to Covidence for screening (Covidence Systematic Review Software, 2023). After 16 duplicates were removed, the titles and abstracts of the remaining 182 articles

were screened, and 126 articles were excluded by title and abstract screening, leaving 56. Eight articles could not be retrieved leaving 48 articles. Then the full texts of the remaining 48 articles were reviewed, 39 were excluded and nine articles met the inclusion and exclusion criteria. Additionally, a citation search identified 12 additional articles, for a final sample size of 21 studies. Search strategies with reasons for exclusion are presented within the PRISMA flow diagram (Figure 1). The 21 articles were critically examined using the Johns Hopkins appraisal tool, and a matrix was created to document each study's methodology, sample and characteristics, themes, design, and recommendations (Table 1).

Results

The reviewed articles on integrative therapies for uterine fibroids were published between 2009 and 2023. Together they represent diverse methodologies and designs, primarily quantitative with six randomized controlled trials. The review had mostly high-quality designs with level 1 research. Studies were conducted in various middle to high-income nations including the U.S. (5), China (2), Taiwan (4), Sri Lanka (1), Finland (1), Italy (4), Egypt (1), and Iran (3). Studies were conducted to examine a variety of integrative methods: Traditional Chinese Medicine (8), Ayurvedic medicine (1), supplements (8), lifestyle modifications (2), and alternative therapy (2). Collectively, the study samples consisted of 217,194 women diagnosed with uterine fibroids and six isolated human uterine fibroid tissue samples.

Traditional Chinese Medicine and Ayurvedic Treatments

Traditional Chinese medicine has been shown to decrease the risk, symptoms, size, and number of fibroids. Yen et al. (2015) did a thorough analysis to determine the Chinese herbal formulae that are most frequently administered for uterine fibroids in Taiwan which included Gui-Zhi-Fu-Ling-Wan (Cinnamon Twig and Poria Pill), Jia-Wei-Xiao-Yao-San (Supplemented

Free Wanderer Powder), Shao-Fu-Zhu-Yu-Tang (Lesser Abdomen Stasis-Expelling Decoction), San-Leng (Rhizoma Sparganii), E-Zhu (Rhizoma Curcumae), and Xiang-Fu (Rhizoma Cyperi). Multiple studies used an herbal remedy instead of one herbal supplementation (Yen et al., 2015; Mehl-Madrona, 2002; Feng & Hong, 2018; Hsu et al., 2019; Meng et al., 2022).

Ten herbal remedies prescribed by Traditional Chinese medicine doctors consistently contributed to a decreased risk of developing uterine fibroids (Hsu et al., 2019). A randomized, double-blind trial (N = 78) comparing the efficacy and safety of the conventional dose of an adapted herbal formula Guizhi Fuling Wan with a sub-effective dose control showed that the size of fibroids was significantly reduced after 16 weeks of treatment (30% vs. 23.7%, $p = 0.001$) (Meng et al., 2022). A randomized, single-blind clinical trial (N = 102) studied the efficacy and safety of two Ayurveda regimens used to treat uterine fibroids compared with a control group and found that a significant decrease in uterine fibroid volume was found in one of the Ayurveda regimens and the fibroid size for the control group increased significantly (Karunagoda et al., 2021). Additionally, a longitudinal study consisted of a Smooth and Shrink Chinese herbal formula consisting of 16 herbs administered for a six-week term and a twelve-week term (Feng & Hong, 2018). The study showed a reduction of uterine size in six out of eight participants, and a reduction of uterine fibroid volume in four out of eight participants, and all but one participant had improvement in fibroid symptoms and quality of life (Feng & Hong, 2018).

In a prospective cohort study of 531 premenopausal women with bothersome fibroids, 34% said that taking herbs significantly reduced their symptoms and had minimal negative side effects (Jacoby et al., 2014). Su et al. (2012) conducted a longitudinal study that investigated the relationship between using TCM and the probability of uterus surgery in women with uterine fibroids. After using TCM for 4.5 years, those given TCM had a five times lower chance of

uterine surgery than those who did not take TCM treatment ($p < 0.0001$). These researchers then conducted a retrospective study of 44,122 patients and showed TCM might potentially treat uterine fibroids at a lower cost than standard Western medicine while also reducing the need for conventional medicine (Su, Muo, & Morisky, 2015).

A pilot study of 37 women treated with either a treatment program (acupuncture, Chinese herbs, nutritional therapy, guided imagery, pelvic bodywork, and meditation) or standard medical approaches concluded there was no notable difference in bothersome symptoms between the groups, indicating nonpharmacological approaches were comparable to pharmacologic approaches (Mehl-Madrona, 2002). Conversely, patient satisfaction was significantly higher among the treatment group. These eight studies conclude that TCM is shown to decrease the risk of fibroids, decrease symptoms of fibroids, decrease the number of fibroids, and decrease the size of uterine fibroids which demonstrates that it could be employed as an alternative treatment for women with uterine fibroids.

Alternative Therapies

In addition to herbal supplementation, other studies researched lifestyle modifications, dry cupping, and acupuncture for managing uterine fibroids. Women said they experienced fewer symptoms after using exercise and nutrition to manage their fibroid-related problems (Jacoby et al., 2014). Vegetable and fruit intake was significantly associated with decreased fibroid risk (He et al., 2013; Wise et al., 2011). He et al. (2013) concluded that an increase in body mass index (BMI) significantly increases the risk of fibroids, while Wise et al. (2011) concluded that increased BMI did not increase the incidence ratio of uterine fibroids.

One case report studied the efficacy of dry cupping therapy in the management of uterine fibroids. When the therapy was over, substantial clinical and sonographic improvements were

observed, including a reduction in dysmenorrhea and vaginal bleeding with no side effects (Dadmehr et al., 2020). Acupuncture has also shown promise in decreasing symptoms related to uterine fibroids with no reported side effects. In an observational study of eight women receiving 7-point Tung's acupuncture twice weekly, there was a reduction in symptoms in 10 of 14 categories after six weeks and a reduction in all 14 categories after the twelve-week treatment (Cruz et al., 2019).

Supplements

This integrative review identified eight articles demonstrating how supplementation use can have a positive effect on women with fibroids. Three articles studied vitamin D as a sole intervention, two studies reported results on vitamin D in combination with ECGC, two studies reported findings from vitamin D in combination with ECGC and vitamin B6, and one study researched ECGC only. Of the articles reviewed on supplementation, only one study showed no statistically significant decrease in uterine fibroid volume. Vitamin D was studied for its effects on decreasing the rate of recurrence, volume reduction, prevention, and symptom management of uterine fibroids (Arjeh et al., 2020; Bläuer et al., 2009; Miriello et al., 2021; Pocaro et al., 2020; Porcaro & Angelozzi 2020; Roshdy et al., 2013; Vahdat et al., 2022). According to a study by Vahdat et al. (2022), a deficiency in vitamin D may be a risk factor for uterine fibroid development, while vitamin D supplementation may prevent fibroid recurrence. This randomized, double-blind pilot study included 109 participants who had undergone a hysteroscopic myomectomy. The control group (n = 54) received a placebo tablet, while the intervention group (n = 55) received vitamin D 1000 IU tablets daily for 12 months. Oral supplementation with vitamin D reduced the recurrence rate of UF by 50% ($p = 0.17$) when compared to the control group. Vitamin D also had a greater size reduction compared to the

control group ($p = 0.73$) (Vahdat et al., 2022). The serum vitamin D levels were remarkably lower in those women who experienced uterine fibroid recurrence when compared to those who did not (Vahdat et al., 2022). Of the women in the intervention group who did not have uterine fibroid reoccurrence, their vitamin D levels were 43.2 (SD = 10.9) compared with those who did have uterine fibroid recurrence 27.2 (SD = 6.6). In the control group, a similar pattern was found. Those who did not have uterine fibroid recurrence had vitamin D levels of 29.9 (SD = 7.8) compared to those who did have uterine fibroid recurrence of 18.3 (SD = 3) (Vahdat et al., 2022).

Moreover, vitamin D has been recognized as a possible anticancer agent since it slows the proliferation of uterine fibroid cells (Arjeh et al., 2020). A randomized double-blind clinical trial (N = 60) studied the effects of oral vitamin D supplementation on uterine fibroid growth. For 12 weeks, the treatment group was given oral vitamin D supplementation of 50,000 IU weekly, while the control group received a placebo. In the experimental group, the volume of the fibroids decreased, though was not statistically significant (mean difference = 0.71, 95% CI = 0.1 to 1.53, $p = 0.085$); however, in the control group, the volume of UFs had significantly increased (mean difference = 2.53, 95% CI = 1.9 to 4.05, $p = 0.001$).

In addition to studying the impact of vitamin D, epigallocatechin gallate (ECGC), the primary catechin in green tea, has also been studied for its potential positive effects as an alternative treatment method for uterine fibroids. ECGC has demonstrated an ability to limit tumor growth by inhibiting key pathways and has reported anti-inflammatory, antiproliferative, and antioxidant effects (Roshdy et al., 2013). In this pilot double-blinded placebo-controlled clinical trial (N = 39), researchers sought to evaluate if oral green tea extract (ECGC) would be safe and effective in treating women with symptomatic uterine fibroids. The treatment group (n =

22) was given 800 mg of green tea extract in capsule form while the control group received a placebo (n = 11). After the four-month study period concluded, the mean total fibroid volume decreased by 32.6 % ($p = 0.0001$) in the ECGC intervention group, while it increased in the placebo group by 24.2%. Additionally, the ECGC-treated group reported a higher increase in health-related quality of life (HRQL) factors (18.73%, $p = 0.01$). The use of EGCG was associated with improvement in bleeding patterns by assessing the mean blood loss every month using a pictogram questionnaire (a decrease from 71ml/month to 45ml/month, $p = 0.001$). In this study, there were not any adverse effects reported by either group (Roshdy et al., 2013).

Four studies have researched the synergistic effects of vitamin D, EGCG, and vitamin B6 on the management of uterine fibroids. In a randomized controlled trial with 30 women with diagnosed uterine fibroids, the treatment group received 25 ug of vitamin D, 150 mg of EGCG, and 5mg of vitamin B6 orally twice daily, while the control group received a placebo (Pocaro et al., 2020). After four months, a 34.7% reduction in the volume of uterine fibroids was noted in the treatment group ($p < 0.0001$), while a 6.9% increase was noted in the control group ($p < 0.001$).

The second study (N = 95) used the same treatment regimen (Miriello et al., 2021). It was concluded that the total volume and peripheral vascularization were decreased by 37.9% ($p < 0.001$) and 7.7% in the experimental group, while an increase in uterine fibroid volume by 5.5% was observed in the control group ($p = 0.83$). The effects of ECGC with vitamin D showed promise in a study by Costabile et al. (2021), where they evaluated the volume and number of uterine fibroids as well as blood loss. The sample size included 19 women who all experienced a significant decrease in uterine fibroid volume at the end of treatment, with an average reduction of 32.72%. While 63% of participants reported heavy bleeding and 37% reported normal

bleeding prior to treatment, this was improved to 5% reporting heavy bleeding and 95% normal bleeding after the treatment period.

In a controlled pilot study by Porcaro and Angelozzi (2021), 22 women were treated twice a day with 25 ug of vitamin D, 150 mg of ECGC, and 5 mg of vitamin B6 for four months. Participants in the treatment group experienced a decrease in the size of uterine fibroids from 10.73 cm³ (SD = 5.52) at baseline to 7.98 cm³ (SD = 4.00) after treatment ($p < 0.0001$). Uterine fibroid volume remained unchanged in the control group (N = 21). Menstrual bleeding and anemia were improved in the treatment group. One uterine fibroid developed in the control group while none formed in the treatment group.

Finally, vitamin D's impact on uterine fibroids has also been tested in an in vitro study (Blauer et al., 2009). The sample size included tissue from six women who underwent hysterectomies for symptomatic uterine fibroids. The early findings demonstrated that normal myometrial and leiomyoma cells in primary and secondary cultures were highly susceptible to the growth-inhibiting effects of 1,25(OH)₂D₃. These research studies consistently demonstrated that oral supplementation with vitamin D, ECGC, and vitamin B6 was safe and effective in managing and preventing uterine fibroids.

Discussion

This integrative review examined the different integrative methods used to manage symptomatic uterine fibroids using the Whittemore and Knafl (2005) framework. The John Hopkins Evidence-Based Practice appraisal tool was used to critically assess each study's methodology, sample and characteristics, themes, design, and recommendation identifying the quality and validity of each study. King's Theory of Goal Attainment focuses on the importance of the relationship between the patient and provider while placing an emphasis on shared-

decision making and patient-centered goals. Educating women on all treatment options for the management of uterine fibroids, including integrative methods, provides women the opportunity to enter shared decision-making with their providers and decide on the treatment option that best aligns with their values and treatment goals. In like manner, researchers found that women with endometriosis were more likely to have sought out complementary and alternative medicine (CAM) therapies for symptom relief than women who do not suffer from endometriosis and accompanying symptoms (Fisher et al., 2016). Furthermore, this research demonstrated that women with premenstrual syndrome had a similar outcome and were more likely to consult with a naturopath/herbalist or an alternative health practitioner to seek out CAM therapies for symptom management (Fisher et al., 2016). These results support the need for further research on integrative approaches to treatment and management of women's reproductive health concerns as women are found frequently seeking out alternative options to mainstream medical treatment.

In this review, all studies demonstrated that integrative management options do have positive effects on uterine fibroids with no reported side effects or adverse outcomes. One management option is supplementation. Outside literature has also found that daily supplementation with vitamin D inhibited the growth of uterine fibroids in human subjects as well as isolated myometrial and leiomyoma tissues (Brakta et al., 2015; Harmon et al., 2022). The serum concentration of vitamin D is believed to play a role in the etiology of primary dysmenorrhea (Zeynali & Haghghian, 2019). While this review had seven studies that showed vitamin D had a positive impact on uterine fibroid size and symptoms, one outside study found that increased vitamin D levels were associated with increased levels of menstrual discomfort. In contrast, another study found that menstrual discomfort was improved with vitamin D and

calcium (Zarei et al., 2017). Additional research is needed to explore the role of vitamin D in the etiology of dysmenorrhea.

ECGC, a powerful antioxidant found in green tea, was found to be a safe and effective alternative treatment for uterine fibroids in this review. Daily supplementation with vitamin D, vitamin B6, and ECGC demonstrated a significant decrease in the volume and symptoms of uterine fibroids (Costabile et al., 2021; Miriello et al., 2021; Porcaro et al., 2020; Porcaro et al., 2021). Comparably, green tea extract has been found to have a positive impact on women with polycystic ovarian syndrome (PCOS) due to its effects on weight loss which results in decreased PCOS symptoms (Maleki et al., 2021). Further research on green tea extract points to its potential benefits in minimizing oxidative stress associated with female infertility. The researchers concluded that it is reasonable for women who suffer from idiopathic infertility to consider oral supplementation with green tea extract ECGC given that it is a potent antioxidant and there are no significant side effects (Roychoudhury, 2017).

Traditional Chinese remedies have documented benefits for women with UFs with few side effects identified. Notably, five studies in this review demonstrated Traditional Chinese Medicine decreases fibroid-related symptoms in women with symptomatic uterine fibroids (Feng & Hong, 2018; Jacoby et al., 2014; Karunagoda et al., 2021; Mehl-Madrona et al., 2002; Meng et al., 2021). These studies were consistent with a systematic review that demonstrated that the Chinese herbal medicine Guizhi Fuling Formula plus mifepristone was more effective than conventional medication mifepristone alone in reducing the volume of fibroids (Chen et al., 2009). Moreover, mifepristone by itself had less of an impact on lowering the volume of all fibroids and the average size of the uterus than did Guizhi Fuling capsule plus mifepristone (Liu et al., 2013).

In addition to supplementation and Traditional Chinese Medicine, this review noted an association between the risk of uterine fibroids and lifestyle changes such as diet and physical activity. Comparably, an outside study by Davis et al. (2023) established that those who consumed the highest amounts of total fruits (≥ 4 /day) were 10% less likely to develop uterine fibroids when compared with those who only had less than one fruit serving per day. It is believed that citrus fruits may reduce the risk of uterine fibroids through pathways mediated by sex hormones, antioxidants, or both (Wise et al., 2011). It was also found in estrogen-related disorders (fibroids, endometriosis, and breast cancer), normalizing estrogen production by maintaining a healthy weight, decreasing inflammation, normalizing glucose and glucose dynamic, and increasing sex hormone binding globulin can decrease the amounts of estrogen within the body (Evans et al., 2008). Consuming more fruits and vegetables combined with a low-animal fat diet can improve symptom management and decrease the risk of uterine fibroids (He et al., 2013; Wise et al., 2011). He et al. 2013 found that a higher-than-normal BMI in premenopausal women had an increased risk of uterine fibroids compared to no associated risk in postmenopausal women due to the decrease in estrogen and the fibroids growth factor IGF-1. Comparatively, a positive correlation between pain intensity and waist circumference, hip circumference, fat percentage, and fat mass were observed which suggests that diet and lifestyle changes can have a positive impact on primary dysmenorrhea (Zeynali & Haghghian, 2019). Based on the studies above, lifestyle modifications, such as increasing fruit and vegetable intake, physical activity, and decreasing BMI, should be recommended to women to support both fibroid management as well as other women's health issues.

Limitations and Strengths of Review

Small sample sizes were a common limitation in most of the reviewed studies. There were also five pilot studies and one case study with low-quality evidence. Additionally, some of the subjects had self-reporting diagnoses of uterine fibroids, and one study where compliance with treatment was unknown. The strengths demonstrated in this review include research articles that were independently screened by two reviewers, included high-quality randomized control trials, and contained literature from a wide range of demographic areas.

Implications for Advanced Practice Nursing Leadership and Practice

Advanced Practice Registered Nurses (APRN's) are leaders in the healthcare industry and they play a vital role in providing care that promotes the overall health and wellbeing of their patients. Health promotion models place an emphasis on disease prevention and can positively empower patients to actively participate in reaching their desired health outcomes. The prevalence of uterine fibroids and the devastating effects it can have on a women's physical and mental health are evident. The research presented in this integrative review serves to inform APRN's of the potential alternative approaches to preventing and managing uterine fibroids. These interventions can be used alone or in conjunction with a medical approach.

APRN's can utilize this information to inform their practice by checking the vitamin D levels of women in reproductive age and recommend supplementation when needed. They can educate on the signs and symptoms of uterine fibroids, so women are aware of what symptoms to report to their provider. They can also recommend diets high in fruits and vegetable and daily supplementation with ECGC. This information is especially useful for those patients who want to utilize a safe, less invasive treatment options. It is imperative that APRN's are well informed on a variety of available options to best support their patients. This will allow them to select the path that best aligns with their preferences and feel supported on their health journey.

Conclusion

The research studies in this review consistently demonstrated the potential positive impact integrative therapies can have on uterine fibroids. The overall recommendation is that more well-designed clinical trials with larger sample sizes and of higher quality be undertaken. Despite needing more research, the results were very promising and there were no adverse events or side effects noted in any of the studies. Providers should consider counseling with these treatments as an option for uterine fibroid management, given that they explain research is still preliminary.

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Figure 1 PRISMA Flow Chart

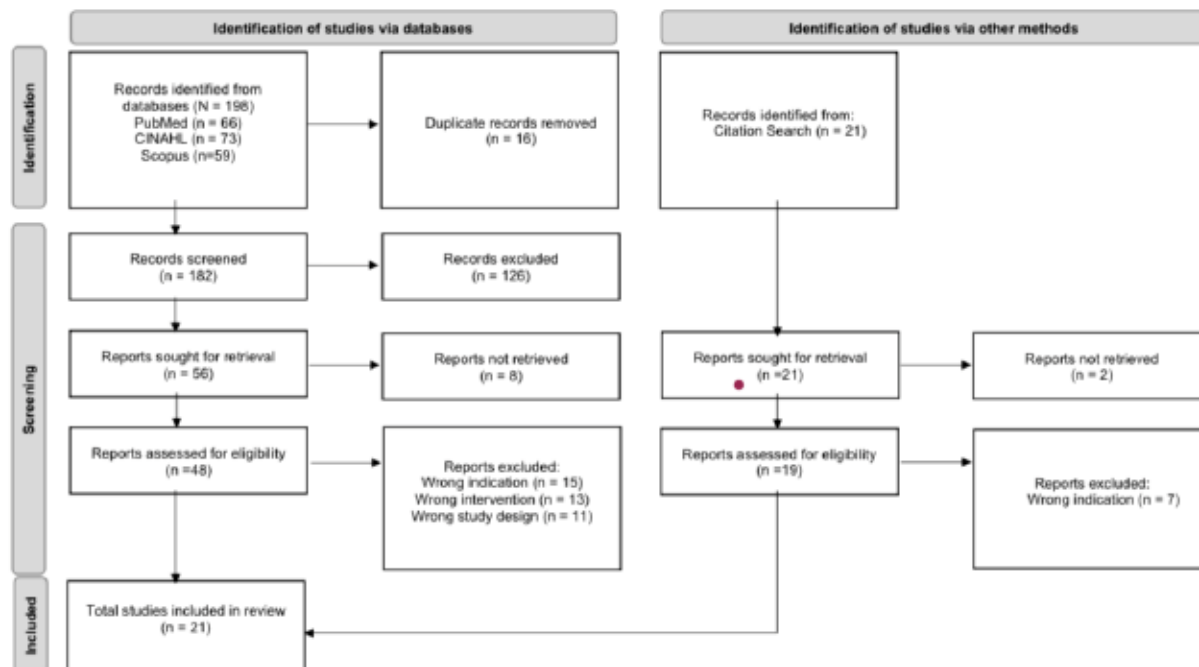


Table 1 Literature Matrix on Integrative Management for Uterine Fibroids

Author (Date)	Purpose	Design	Sample	Results	Recommendations	Level, Quality
Arjeh, S., Darsareh, F., Asl, Z. A., & Azizi Kutenaeei, M. (2020)	To investigate the effect of vitamin D on uterine fibroids.	Randomized clinical trial	55 women with uterine fibroids	While no reduction or increase in fibroid size was observed in the experimental group, fibroid size in the control group increased.	Further research should explore the long-term effects of treatment with vitamin D.	Level 1 Good quality
Bläuer, M., Rovio, P. H., Ylikomi, T., & Heinonen, P. K. (2009)	To determine the effect of 1,25(OH) ₂ D ₃ and 25(OH)D ₃ vitamin D derivatives on the growth of leiomyoma and myometrial cells in vitro.	Experimental In Vitro Study	6 premenopausal women with uterine leiomyomas	In both myometrial and leiomyoma cells, D ₃ inhibited growth by 12 % when compared to the control group	More research is needed to find out whether women with hypovitaminosis D also have more uterine leiomyomas than women with efficient vitamin D supplies.	Level 1 Good
Costabile, L., Burratti, M., Biovi, G., Pajalich, R., & Unfer, V. (2021)	To evaluate the efficacy of	Observational Cohort study	19 women with uterine fibroids	All the patients experienced a significant decrease in uterine fibroid volume	Supplementation with EG-CG, vit D ₃ , and vit B ₆ reduced the size of uterine fibroids	Level 3 High Quality

	the combined supplementation of EGCG with vitamins (vit) D3 and B6 on the reduction of volume and blood loss related to UF.			treatment. A significant reduction in blood loss was reported by patients at the end of the study.	and the abnormal heavy bleeding. Therefore, this novel combination could be an alternative approach for uterine fibroid reduction and the correlated symptoms.	y
Cruz, J., Carrington, L., & Hong, H. (2019)	To assess the treatment of uterine fibroids (UFs) and related symptoms with a 7-point Tung's acupuncture protocol.	Prospective Cohort	8 participants with uterine fibroids	After 12 weeks of treatment, 9 of the 14 surveyed symptoms were completely eliminated.	The study also suggests that acupuncture might reduce symptoms related to uterine fibroids.	Level 4 Low Quality
Feng, S., Hong, H. (2018).	To observe the	Longitudinal Observatio	10 participants with	The Chinese herbal formula, Soothe & Shrink, may reduce	S&S formula may be a safe and promising	Level 3

	effect of the Chinese herbal formula , Soothe & Shrink, on the treatment of uterine fibroids.	nal Pilot Study	uterine fibroids	the uterine size and fibroid volume and improve the clinical symptoms and quality of life of uterine fibroid patients.	alternative to hormonal therapy and surgery for uterine fibroid patients.	Low quality
He, Y., Zeng, Q., Dong, S., Qin, L., Li, G., & Wang, P. (2013)	To investigate the associations between uterine fibroids and lifestyles including diet, physical activity, and stress.	Observational Case-control study	73 women with uterine fibroids and 210 women without fibroids.	It was concluded that vegetable and fruit intake and occupational intensity significantly decreased the risk of fibroids; Conversely, increased BMI significantly increased the risk of uterine fibroids in women.	Vegetable and fruit intake and occupational intensity had positive effects on uterine fibroids, and a high BMI increased the risk of fibroids in premenopausal women.	Level 3 Moderate
Hsu, W.-C., Tsai, Y.-T., Hou, Y.-C., & Lai, J.-N. (2019)	To compare Chinese Herbal Product (CHP) users with those who do not use CHPs.	Population-based cohort study	52,151 participants	CHPs seem to contribute to a decreased risk in developing uterine fibroids. Findings suggest that CHP care might be beneficial to prevent women from developing uterine fibroids.	Accuracy assessment of efficacy requires further study. Additional double-blind, randomized, placebo-control studies are needed to determine the efficacy	Level 3 Good Quality

Jacoby, V. L., Jacoby, A., Learman, L. A., Schembri, M., Gregorich, S. E., Jackson, R., & Kuppermann, M. (2014).)	To examine the use of medical management, uterus-preserving surgery (UPS), and complementary treatments among women with uterine fibroids.	Prospective cohort study	933 premenopausal women with symptomatic fibroids	UPS are effective treatments for women with fibroids, but many women use hormonal or complementary treatments and report significant symptom improvement without surgical intervention. CAM was also commonly used to relieve fibroid-related symptoms, and 38–46% reported that these treatments made their symptoms “a lot better.”	Nonsurgical management may be a viable option for many women and medical treatment, including CAM, may significantly improve symptoms. Further research on the effectiveness of Western medication and CAM, as well as expectant management, is needed to better inform counseling for women who wish to avoid surgery.	Level 2 Good
Karunagoda, K. P. K.R., Perera, P. K., Senanayake, H., & De Silva Weliange, S. (2021)	To assess the efficacy and safety of two Ayurveda drug regimens for the treatment of uterine fibroids (UF).	Randomized Single-Blind Clinical Trial 2 experimental groups and 1 control group	120 participants with uterine fibroids	A significant decrease in the volume of UF was observed in one of the experimental groups, while a significant increase in the volume of UF was observed in the control group in the 12th week.	Multicentered randomized controlled trials are needed to confirm these findings.	Level 1 Good
Dadmehr, M, Ayati, M.H.,	To determine	Case Study	1 Woman with AUB,	After two months, women experienced	More research is needed	Level 5

Rostami, S, & Akhtari, E. (2020)	ne if dry cupping therapy can be an effective and safe therapy for decreasing fibroid related symptoms and fibroid size.		dysmenorrhea, and large UF	a decrease in dysmenorrhea and vaginal bleeding and a decrease in the size of uterine fibroids.		Poor
Mehl-Madrona, L. (2002)	To determine the efficacy and cost of a suite of alternative therapies (Traditional Chinese medicine, body therapy, guided imagery) for the treatment of uterine fibroids and their	Quasi-Experimental Pilot study	74 women with uterine fibroids	Fibroids reduced in size or stopped growing in 59% and 8% of the comparison group.	More research is needed using a randomized, controlled trial with subjects not actively seeking complementary therapies.	Level 3 Low Quality

	associated symptoms.					
Meng, W., Lin, W. L., Yeung, W. F., Zhang, Y., Ng, E. H. Y., Lee, Y. P. E., Zhang, Z.-J., Rong, J., & Lao, L. (2022)	To study the efficacy and safety of the conventional dose of a modified herbal formula Guizhi Fuling Wan in patients with symptomatic uterine fibroids.	Randomized double-blind study	78 women with symptomatic uterine fibroids	The low-dose group yielded greater endpoint improvement in the Chinese medicine syndrome score than the conventional-dose group ($p = 0.024$).	The herbal formula Guizhi Fuling Wan was shown to be safe in women with uterine fibroids.	Level 1 High-Quality
Miriello, D., Galanti, F., Cignini, P., Antonaci, D., Schiavi, M.C., Rago, R. (2021)	To determine the effect of oral supplementation with a combination of vitamin D plus epigallocatechin gallate	Experimental study Treatment and control group	95 women with uterine fibroids	After treatment, myomas' total volume and peripheral vascularization significantly decreased respectively by 37.9%, increased in myomas' volume by 5.5 %, and peripheral vascularization by 5% in the control group.	Future randomized double-blinded controlled studies with larger groups of women affected by fibroids are needed, including different ethnic groups.	Level 1 High-Quality

	(EGCG) and vitamin B6 in women with myomas.					
Porcaro, G., Angelozzi, P. (2021)	To evaluate the efficiency of the combination (vit D, ECGC, vit B6) to improve gynecological and cardiologic parameters.	Controlled Pilot Study	43 women with a diagnosis of uterine fibroids	UF size decreased, menstrual bleeding decreased, and anemia ameliorated after 4 months of treatment in the treatment group.	Further research is needed for validating these preliminary results. More randomized controlled trials with a larger cohort of patients, including different ethnic groups, are needed.	Level 1 Good quality
Porcaro G., Santamaria A., Giordano D., & Angelozzi P. (2020)	To verify the effect of combined oral vitamin D and ECGC supplementation in	Pilot Study	30 women with myomas	The total myoma volume significantly decreased by 34.7% in the treated group, whereas it increased by 6.9% in the control group.	Further controlled studies, with a larger randomized cohort and different ethnic groups, are required to validate these encouraging results.	Level 1 Good

	symptomatic women with myomas.					
Roshdy, E., Rajaratnam, V., Maitra, S., Sabry, M., Allah, A. S., & Al-Hendy, A. (2013).	To evaluate the efficacy and safety of green tea extract (epigallocatechin gallate [EGCG]) on the burden and quality of life in women with symptomatic uterine fibroids.	Double-blind randomized control pilot study	39 women with uterine fibroids	In the placebo group, fibroid size, increased by 24.3%, while those randomized to green tea extract treatment showed a 32.6% in a total reduction of uterine fibroid volume.	More research is needed to confirm these results; larger multicenter trials are needed.	Level 1 Good Quality
Su, S.-Y., Muo, C.-H., & Morisky, D. E. (2012).	To investigate the association between the use of CM and the incidence	Retrospective Cohort Study	16,690 women diagnosed with a uterine fibroid	Incidence of uterine surgery was significantly lower in CM users than CM nonusers ($p < 0.0001$).	Further large clinical trials are obviously required to evaluate the dimension of benefits that CM could provide.	Level 3 Good Quality

	ce of uterine surgery in women with uterine fibroids.					
Su, S.-Y., Muo, C.-H., & Morisky, D. E. (2015).	To compare the consumption of conventional Western medicine and medical cost between Chinese medicine (CM) users and nonusers among patients with uterine fibroids.	Retrospective Cohort Study	44,122 patients; 11,412 patients were identified as CM users, and 32,710 patients were identified as CM nonusers.	This study revealed that CM reduced the consumption of conventional medicine commonly used to release symptoms of fibroids.	CM might be a potential therapeutic substitute for conventional medicines to treat uterine fibroids at low cost.	Level 3 Medium Quality
Vahdat, M., Allahqoli, L., Mirzaei, H., Giovannucci, E., Salehiniya, H., Mansouri, G., & Alkatout, I. (2022)	To investigate the effect of vitamin D supplementation on	Randomized, double-blind, placebo-controlled pilot study	109 women who had undergone hysteroscopic myomectomy	The administration of vitamin D supplements for one-year reduced recurrence rates of UFs by 50%.	vitamin D appears to be a promising and safe agent in the prevention of recurrence and reduction of the size of recurrent UFs.	Level 1 Good Quality

	the recurrence of UFs.					
Wise, L. A., Radin, R. G., Palmer, J. R., Kumanyika, S. K., Boggs, D. A., & Rosenberg, L. (2011)	To assess the association of dietary intake of fruit, vegetables, carotenoids, folate, fiber, and vitamins A, C, and E with uterine fibroids in the Black Women's Health Study.	Prospective Cohort study	59,000 African American women	Fruit and vegetable intake was inversely associated with uterine fibroid risk. Dietary vitamin A (1g/d RAE) was inversely associated with UL risk.	High intake of fruit, particularly citrus fruit, was inversely associated with uterine fibroid risk among black women. An inverse association was also found for dietary intake of vitamin A derived from animals but not vegetable sources.	Level 2 Good quality
Yen, H.-R., Chen, Y.-Y., Huang, T.-P., Chang, T.-T., Tsao, J.-Y., Chen, B.-C., & Sun, M.-F. (2015)	To investigate the utilization of Chinese herbal products for patients with	Population based Study	35,786 newly diagnosed subjects with uterine fibroids	Gui-Zhi-Fu-Ling-Wan (Cinnamon Twig and Poria Pill) was the most frequently prescribed Chinese herbal formula, while San-Leng (Rhizoma Sparganii) was the most commonly	Further basic mechanistic studies and clinical trials are needed to confirm the therapeutic effects and mechanisms of CHP.	Level 3 Good Quality

	uterine fibroid.			prescribed single herb.		
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