



## COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) THERAPIES FOR MANAGEMENT OF PAIN RELATED TO ENDOMETRIOSIS

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### ABSTRACT

Endometriosis is a gynaecological disease with a complex etiology. It is associated with severe pelvic pain, sub fertility and reduced quality of life. Endometriosis has a multifactorial etiology and therefore its management is also multidimensional. The main targets of therapy are controlling of the pain symptoms and increasing fertility where it is desired. Hormonal and surgical therapies are the two major treatment modalities available currently. But they are not without their side effects. Therefore many women explore Complementary and Alternative Medicine (CAM) forms of treatment for symptomatic relief from pain. These CAM therapies have been used as an adjuvant to conventional therapy or as an independent form of treatment. CAM therapies are purported to have lesser side effects as compared to conventional medical formulations. Ancient Chinese and Indian medicine system have laid the foundation of several of the prevalent Cam practices. The following CAM practices have been discussed in the article-Acupuncture, Herbal therapy, Meditation and Hypnotherapy, Yoga, Exercise, Dietary therapy Aromatherapy and Massage, Reiki, Magnet therapy and Chiropractic. Randomized Clinical Trials (RCT) have been conducted for some of the CAM therapies in Endometriosis and Acupuncture and Herbal and Dietary therapies have been found to have some positive effect on the patients. The efficacy of CAM therapies still needs substantial evidence to be integrated into general healthcare practices.

**Keywords:** Complementary medicine, CAM, Endometriosis, Dysmenorrhea, Pain Management

### INTRODUCTION

Endometriosis was first “discovered” by surgeon Thomas Cullen in 1920<sup>1</sup>. He named the condition Adenomyoma and mentioned about the classical ectopic sites where endometrial like tissue were found. The name “Endometriosis” was coined by John A Sampson after his paper on Ovarian Endometriomas<sup>1</sup> and he was the first to describe the pathogenesis of the condition. There are several theories on the pathogenesis of Endometriosis and they could be classified under three broad categories<sup>2</sup>. Firstly, the in situ development by hormonal induction, secondly, the Implantation theory which involves retrograde menstruation and thirdly a combination of both the above processes. Clinically, Endometriosis is defined as the presence of Endometrial like tissue outside the uterus, which induces a chronic, inflammatory reaction and results in pelvic pain, Dysmenorrhea, dysuria, dyspareunia and dyschezia. Endometriosis is an estrogen-dependent disorder and occurs generally in women of reproductive age group. The prevalence of endometriosis is estimated up to 10% in the general population and for women with sub fertility the prevalence rate ranges from 25% to 40%<sup>3,4</sup>. The true prevalence of endometriosis is not known for several reasons. First, the pain symptoms do not correlate well with the disease severity. Women are taken to think that pain during menstruation is “normal”. This could be due to lack of awareness<sup>5</sup>. Secondly, the lack of any reliable, entirely conclusive, effective and non-invasive diagnostic/screening tool makes early diagnosis and management difficult. Currently, laparoscopy which is an invasive procedure is the gold standard for diagnosis.

The management of endometriosis has perplexed physicians in the earlier days and some had recommended early marriage and frequent child bearing as a prophylactic measure<sup>6</sup> for the avoidance of this condition. We have come a long way from such impractical suggestions. However,

endometriosis is difficult to cure completely, and treatment would involve management of pain symptoms effectively so as to increase the quality of life.

### Current Conventional Therapy Modalities Include

**Pharmacologic based therapies** - It involves hormonal therapy like gonadotropins release hormone (GnRH) agonists, oral contraceptive pills, progestogens and androgen derivatives and a few newer alternatives like the selective progestogen receptor modulators, aromatase inhibitors and GnRH antagonists<sup>7</sup>. All the above therapies either work by suppressing the menstrual cycle, inhibiting ovarian function by the suppression of estrogen release or by decreasing myometrial activity. Non-hormonal pharmacological based therapies include non steroidal anti inflammatory drugs (NSAID) as the first line therapy for pain management owing to their Cyclooxygenase (COX) 1 and 2 suppressing properties (suppress prostaglandin synthesis, which, in turn, can inhibit pain potentiation by other mediators like histamine and bradykinin) along with other COX independent effects like induction of apoptosis, cell growth suppression, inhibition of angiogenesis and inhibition of metastasis<sup>8</sup>. But the recurrence rate is almost 70 % for NSAIDs<sup>9</sup>. Side effects for all the above mentioned therapies may include either or of the following symptoms: androgenic effects, hirsutism, weight gain, nausea, mild bloating and altered mood swings. Other non hormonal promising therapies include angiogenesis disruptors and immune modulators but they need further insight<sup>7</sup>.

**Surgical based therapies** - They could be of two types – Conservative surgery or Radical surgery. Major objective of conservative surgery is to ablate or excise all visible or diffused lesions and it includes<sup>10</sup>:

- i) Laparoscopy with surgical excision of lesions
- ii) Laparotomy with surgical excision of lesions

Radical surgery might be required in extreme cases where the progress of lesions is extensive and in older patients with planned families. It includes:

- i) Hysterectomy with ovarian Conservation
- ii) Hysterectomy with removal of ovaries

Surgeries do provide symptomatic relief but may give rise to associated complications in 2-3% of the cases as reported by a particular study. Also the recurrence rate is close to 44% after conservative laparoscopic surgeries<sup>11</sup>.

Owing to the side effects found in the conventional approach, many women are turning to other complementary and/or alternative medicine (CAM) for pain relief in endometriosis. Ease of administration, lots of available options and economically cheaper medication have been the reasons why CAM therapies are favoured by women.

#### **Complementary and Alternative Medicine (CAM)**

CAM is defined by the NIH - National Center for Complementary and Alternative Medicine (NCCAM) as a group of diverse medical and health care systems, practices, and products that are currently not integrated into conventional medicine<sup>12</sup>. The National Institutes of Health has classified CAM in 5 ways:

- (1) Alternative medical Systems like Acupuncture, Naturopathic Medicine, Ayurveda and Homeopathy.
- (2) Biologic-based therapies including herbal and dietary therapies.
- (3) Energy therapies, such as Reiki, therapeutic touch, magnet therapy etc.
- (4) Manipulative and body-based systems like chiropractic, osteopathy, and massage.
- (5) Mind-body interventions, such as meditation, biofeedback, hypnotherapy, and the relaxation response.

This mini review looks into all the prevalent CAM practises in Endometriosis, brief description of their mode of action and discusses about their efficacy in relieving pain associated with Endometriosis. Most of the practises are aimed at providing symptomatic relief to the women and improve overall sense of well being. All the therapies discussed belong to either one of the five categories mentioned above.

#### **METHODOLOGY**

A PubMed search was performed in January 2012 by using the search terms "CAM", "Complementary and Alternative Medicine" in conjunction with the key words "Endometriosis" and "Dysmenorrhea" and "Pain". Additional PubMed searches were performed using the names of specific CAM therapies with "endometriosis" and "pain". Articles in English language were selected for the review. Bibliographies of the selected articles were also looked into for any further relevant references.

#### **Acupuncture**

Acupuncture in one of the ancient healing practices followed within the Traditional Chinese Medicine (TCM) system. There are several different forms of acupuncture therapy based on the parts of the body subjected to needles<sup>13</sup>. For example, there is the

- 1) Body acupuncture, where points on the human body along the traditional meridians but excluding the cranium and the ears are pierced.
- 2) Scalp acupuncture – insertion of needles into the scalp for treatment of neurological disorders.
- 3) Auricular acupuncture – insertion of needles into the points in the ears.

There is also Electro Acupuncture, (also known as Percutaneous Electrical Nerve Stimulation PENS) which uses electrical current to stimulate the acupuncture points. According to the ancient TCM, disruption to the flow of vital energy Qi (whose literal translation means breath, air, or gas) in the body leads to diseases and pain. Application of Acupuncture is believed to unblock those energy channels and rectify the imbalance. Though exact mechanism of action is not clear, it is believed that acupuncture influences body's naturally occurring pain mediators like  $\beta$ -endorphin. It induces visceral and somatic signals that lead to increase in endogenous opioids and neurotransmitters like serotonin and dopamine, causing analgesia and sedation. Acupuncture was found beneficial for women with Dysmenorrhea through its influence on the  $\text{PGF}_{2\alpha}$  levels in menstrual fluid. Other studies indicated that its main therapeutic action is by elevation of plasma  $\beta$  endorphins levels and co ordination of uterine activity.

In an exhaustive review<sup>13</sup>, it was summarized that larger studies involving Randomized Clinical Trials (RCT) of acupuncture therapy needs to be done. Although acupuncture is one of the oldest forms of therapy to seek relief from several pain conditions, more research is required in the area of comparison between acupuncture and other conventional forms of medicine. Currently the effectiveness of acupuncture in relieving pain associated with endometriosis is debatable. High quality RCTs and proper intervention measures need to be standardized to validate its use and efficacy.

#### **Herbal therapies**

In TCM, Endometriosis is considered to be arising out of a blood stasis syndrome and its cures are targeted to resolve this problem. The drugs that are generally used have several active components with anti inflammatory, anti proliferative and anti analgesic properties. Some of the herbs that are most commonly used are Cinnamon Twig, Myrrh, Chinese Angelica and Licorice Root. A detailed list of herbs with their English and Chinese names along with their active components is available<sup>14</sup>. Several of the herbs were shown to have an effect on the cytokine expression. Especially curcumin was shown to suppress NF-Kappa  $\beta$  which is a pro-inflammatory pathway<sup>14</sup>. Other herbs like Cinnamon and Licorice roots were shown to inhibit the prostanoid system which is involved in the production of  $\text{PGE}_2$ , a potent stimulator of Aromatase which is a key regulator in endometriosis. Chinese Angelica has a potent anti-oxidant effect<sup>14</sup>. Despite gaining popularity among patients with endometriosis, Chinese herbal medicines which are dispensed as cocktails of various herbs, run the risk of adverse toxicity and herb drug interactions<sup>11</sup>. Current evidence based literature lacks data in this area. Standardization of dosage and efficient regulation mechanisms need to be put in place for safer herbal therapies.

#### **Homeopathy**

Homeopathy, which relies on the cardinal principle of "treating like with like" (first mentioned by Hippocrates) was first propounded by Dr. Samuel Hahnemann (1755-1843), in the year 1796<sup>15</sup>. Sepia (ink of cuttle fish), Cuprum metallicum (copper) and Nux vomica (poison nut) are used as homeopathic cures for Dysmenorrhea. Ipecac root, Belladonna and sepia are found to be especially useful in endometriosis<sup>15</sup>. Homeopathy could be used as first line of treatment. Conducting RCTs in homeopathy is difficult as the

therapy is individualised taking into account all aspects of the patient's condition, lifestyle and personality. Also, the same condition in different patients could be treated by different medication by different practitioners. It was reported that severity of disease decreased and quality of life increased in patients suffering from dysmenorrhoea after homeopathic treatment<sup>16</sup>. Homeopathy is very popular in India and Germany for its holistic approach.

#### **Meditation and Hypnotherapy**

There is no study done to suggest efficacy of meditation in endometriosis related pain but other studies have found that there is a place for mindfulness meditation (Vipassana) in managing chronic lower back pain<sup>17</sup>. The principle of Vipassana is that the meditator remains awake and alert and concentrates on his breath in its entirety. Meditation could be least helpful of all CAM therapies and it is more of a tool to increase pain acceptance and pain threshold. It might also help in improved compliance to other conventional therapies.

Hypnotherapy was reported in one of the studies where TCM and Hypnotherapy were used in conjunction to develop a holistic therapy called SART- Systemic Auto Regulation Therapy and it was used to help a patient suffering from endometriosis<sup>18</sup>. Individualized acupuncture was used to induce trance in SART. Patients visualise images and memories in their trance like semi-conscious state. While the patients are emotionally destabilised, needles are inserted into various acupuncture points. The authors reported improvement in well being and pain symptoms following therapy. But absence of a control group for comparison and the subjective nature of effectiveness pose serious limitation to the study.

#### **Yoga and Exercise**

Yoga is an ancient Indian practice which employs a combination of Asanas (postures) and Pranayama (breathing techniques) that help in achieving mental balance and creates mind body harmony and a general spirit of well being. The suggested mechanism of action of yoga is an increase in tissue flexibility, decrease in sympathetic nervous system activity, reduction in inflammatory markers and increased secretion of endorphin<sup>19</sup>. Yoga has been found to alleviate pain in Migraines, headaches and backaches. 3 yogic poses – The Cobra pose, The Cat pose and the Fish pose have proven effective in primary Dysmenorrhoea<sup>20</sup>. Yoga may not serve immediate noticeable benefits but its regular practice might improve spinal flexibility and strengthens the pelvic floor muscles which will help in pain tolerance. More RCTs need to be done to reach a definite judgement.

Exercise has also been suggested for prevention and cure of symptoms associated with Dysmenorrhoea. Physical exercise involving 30 minutes of continuous walking or jogging and regimens that stretch the connective tissue around the pelvis have gained interest as they have shown to decrease pain symptoms. Aerobic exercise stimulates the release of endorphins which act as an analgesic for non-specific pain<sup>21</sup>. But using exercise as a therapeutic intervention could pose challenges as quality, intensity and duration need to be quantified and standardized. Some studies have suggested an inverse relation between the level of physical exercise and endometriosis. They claim that physical exercise might have a protective effect as it increases the levels of sex hormone binding globulin and reduces bioavailable estrogen<sup>22</sup>. Endometriosis being an estrogen dependent disorder, would

respond favourably to interventions that lower the levels of estrogen. More studies need to replicate these findings.

#### **Dietary Therapy**

Thiamine (Vitamin B<sub>1</sub>) has been studied extensively as a dietary supplement for dysmenorrhoea and found to be very effective<sup>11</sup>. Vitamin E might lead to pain relief by suppressing arachidonic acid release and reducing prostaglandins formation. Magnesium and Omega 3 Fatty Acids are also suggested dietary supplements for pain relief. Omega 3 fatty acids found in fish oil, Canola oil, wheat germ oil lead to formation of less pro active inflammatory eicosanoids like PGE<sub>3</sub> and PGE<sub>3a</sub> hence they might decrease painful menstruation<sup>23</sup>. More fibre intake to increase excretion of estrogen and reduction of dietary fat to reduce serum estrogen levels might prove beneficial. It is also advisable to reduce intake of Vitamin D and Omega 6 Fatty Acids. Vitamin D influences local activity of immune cells and cytokines maintaining endometriosis and Omega 6 Fatty Acids contribute to pro inflammatory eicosanoids like PGE<sub>2</sub>, PGF<sub>2a</sub> and Leukotrienes<sup>24</sup>. Consumption of milk, liver, carrots, cheese, fish and whole grains along with coffee and alcohol were not significantly related to endometriosis in a study by Parazinni et al<sup>25</sup>. Certain nutraceuticals which are bioactive plant compounds like resveratrol, a polyphenol present in red-wine and grape-seed, epigallocatechin-3-gallate (EGCG) from green tea and curcumin from Curcuma longa have been found to have an effect in modulating angiogenesis<sup>26</sup> and thus could prove beneficial in Endometriosis also.

#### **Antioxidants rich Diet**

Oxidative stress might play a role in the development and progression of endometriosis. High concentration of Reactive Oxygen and Nitrogen Species (RONS) were found in the milieu of peritoneal fluid of women with endometriosis. One of the interventions included feeding the women with a high anti oxidant diet<sup>27</sup>. The study compared the anti oxidant intake through diet of women with endometriosis and those without it. Also, the intervention intended to find the capacity of decreasing oxidation markers in the peripheral blood of women with endometriosis after being fed with a diet rich in Vitamin A, C and E derived from vegetables, fruits and seeds. It was found that at the end of the study period, women had decreased peripheral concentration of free radicals.

#### **Aromatherapy and Massage**

Aromatherapy involves the use of essential oils derived from plants. These oils are pleasant smelling and are generally used in massages. Massage involves the use of soft tissue manipulation using pressure by fingertips<sup>28</sup>. Aromatherapy and massage are simple and safe procedures to provide relief from endometriosis associated pains, though the extent of pain relief could vary among subjects. Aromatherapy triggers the limbic system which might help in alleviating the pain<sup>29</sup>. Topical application of essential oils to the lower abdomen and back followed by massage may improve the blood circulation and reduce the spasms that cause pain.

#### **Energy based therapies – Reiki and Magnet based therapies**

Reiki is an energy based CAM modality. Reiki treatments tap into the healing, all sustaining living energy and making it available through touch. During a Reiki session, the practitioner acts as a channel to transfer the all pervading energy into the client's body using his own hands. Reiki

could be explored as a medium for pain relief though there is no study till date involving use of Reiki in healing endometriosis associated pain<sup>30</sup>. Research in Reiki is mostly anecdotal and lacks the scientific rigor of evidence based medicine.

The healing power of magnets was discovered by ancient Greeks. General use of magnets could include relief from pain, reduction of inflammation and improved circulation<sup>31</sup>. These functions could be explored in Endometriosis pain management as increased blood circulation will remove the pain mediators and restore natural balance. One RCT studied the effect of a 0.27 T static magnet attached over the pelvic area, compared with a placebo magnet in women with primary dysmenorrhea and reported significant reduction in pain symptoms<sup>32</sup>. However, there are no RCT s done till date exploring the efficacy of magnets in endometriosis but it is worth being looked into.

### Chiropractic

It is one of the most commonly used branches of the CAM which is concerned with the diagnosis, treatment and prevention of disorders of the neuromuscular skeletal system and their effects on general health<sup>33</sup>. Most common technique of treatment in Chiropractic is the spinal adjustment or manipulation. In a spinal manipulation, a sudden force is employed and with the help of a passive manual manoeuvre, a controlled thrust is delivered at the joint complex so as to take it beyond its normal range of articulation without hurting it. These techniques must be administered by trained professionals keeping in mind the biomechanics and physics of the joints. It is hypothesized that when the nervous system is not functioning properly, the electromagnetic energy associated with it is also imbalanced. Dysmenorrhea which is pelvic visceral disorder could arise due vaso-constriction and congestion. A chiropractor could administer a spinal manipulation to increase spinal mobility through manipulation of lower vertebrae and influence the sympathetic and para sympathetic nerve supply associated with the blood vessels and increase blood circulation, thus leading to pain relief. Another hypothesis supports the thought that dysmenorrhea is the referred pain from lumbar spine, pelvis and hips and the pain from these structures is affected by cyclical hormonal changes in the body<sup>33</sup>. Hence chiropractic dealing with this pain could effectively treat pain during menstruation too.

No data is currently available to conclusively advocate the efficacy of spinal manipulation in dysmenorrhea but as it is one of the most sought after CAM modalities, its popularity may continue despite the lack of scientific proof.

### CONCLUSION

Conventional, as well as complementary medicines have their own strength and weaknesses. It might be erroneous to single out any one kind of therapy as the best option. Especially, in a chronic disease like Endometriosis with its complex, multifactorial etiology, it is difficult to nail down a panacea. Under such circumstances, CAM therapies which are patient compliant, albeit to different extents could be used in combination with conventional treatment options.

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