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Review Article

The Effectiveness of Curcumin on Dysmenorrhea

Shubhangi Shrivastav*, Ravindra Tyagi, Meenakshi Singh, Sudhanshu Jha

Department of Pharmacy, Vishveshwarya Group of Institutions, G.T. Road Greater Noida Phase II Noida, Uttar Pradesh 203207

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*Address for Correspondence:

Ms. Shubhangi Shrivastav, Assistant Professor, Department of Pharmacy, Vishveshwarya Group of Institutions, G.T. Road Greater Noida Phase II Noida, Uttar Pradesh 203207

Abstract

Menstruation is a cycle of oocyte release and preparing uterus for possible pregnancy if fertilization occurs. It begins at puberty and ends at menopause with an average duration of 28 days. Primary menstrual pain is a problem for women throughout the world that can affect daily life. Painful menstruation, also known as dysmenorrhea, is one of the most common women's problems. Most women begin having dysmenorrhea during adolescence, usually within four to five years of the first menstrual period. Painful periods become less common as women age. For the treatment of dysmenorrheal much herbal medicine are use. Curcumin is one of the best phytochemical which is isolated from *Curcuma longa* L., is a fat-soluble natural compound which accumulative evidences have demonstrated that it can use to treat dysmenorrhea. The objective of this paper is to analyze through literature regarding primary dysmenorrhea and natural herbal used to relieve the pain. Data from previous research show that curcumin and is the best candidates for relieving primary menstrual pain.

Keywords: Menstrual cycle, Dysmenorrhea, Curcumin, *Curcuma longa*

Introduction

Female menstrual cycle happens to allow ovum released from the follicle and to prepare the uterus for possible pregnancy. It starts at puberty, between the ages 10-16, and ends at menopause around 51. One menstrual cycle usually occurs from 21 days to 35 days, with an average length of 28 days¹. Menstrual pain (dysmenorrhea) is cramping from the uterus that occurs during menstruation².

There are two types of dysmenorrhea: primary and secondary³. Primary dysmenorrhea is menstrual pain that occurs in the absence of gynecological disease. It usually starts from the sixth to twelve months after menarche (first menstruation) and it is possible to continue until menopause⁴. Primary dysmenorrhea usually begins around the beginning of menstruation and continues for 8 to 72 hours⁵. Secondary dysmenorrhea probably occurs at any time between the menarche and menopause phases. Usually, it happens after the age of 25 years due to gynecological pathologies such as endometriosis and ovarian cysts. The prevalence of primary dysmenorrhea is widespread throughout the world. More than 50% of menstrual women around the globe are reported suffering dysmenorrhea, with 10-20% of them having severe pain. It affects their activities because they cannot work nor do other activities for 1-3 days^{4, 6}. In Indonesia, about 54.8% of females having primary dysmenorrhea, and 9.36% having secondary dysmenorrhea⁷. The symptom of dysmenorrhea can include premenstrual symptoms, mood swings, stomach cramps, headaches, backaches, nausea, and vomiting^{6, 8}. Various attempts were made to alleviate the pain of primary dysmenorrhea. Non-pharmacological efforts were also carried

out including hot water bottles⁹, exercise⁹⁻¹³, acupuncture¹⁴, yoga¹⁵, physiotherapy^{12, 16}, using fruits¹⁷, and herbs¹⁸⁻²². This review is focused on exploring the benefits and how effective the curcumin as herbal medicine to relieve the pain during menstruation based on literature review.

Dysmenorrhea symptoms

The pain of dysmenorrhea is crampy and usually located in lower abdomen above the pubic bone (the suprapubic region); some women also have severe pain in the back or thighs. The pain usually begins just before or as menstrual bleeding begins, and gradually diminishes over one to three days. Pain usually occurs intermittently, ranging from mild to disabling. Other symptoms that may accompany cramping include nausea, diarrhea, dizziness, fatigue, headache, or a flu-like feeling.

Dysmenorrhea diagnosis

The diagnosis of dysmenorrhea is based upon a woman's medical history and physical examination.

Physical examination- Women with dysmenorrhea should have a complete abdominal and pelvic examination. During the examination, the health care provider will observe and feel the size and shape of the vagina, cervix, and uterus, and attempt to feel the ovaries. An internal pelvic examination may not be necessary in adolescent girls.

Other tests - In some women, pelvic ultrasonography (performed vaginally if possible) can be useful in determining

if conditions such as uterine fibroids, uterine adenomyosis, or endometriosis are present.

What happens in the female body during menstruation

Menstruation is a cycle of degeneration of the uterine lining as a response to interaction among hormones produced by the hypothalamus, pituitary, and ovaries. The length of the menstrual cycle is the number of days between the first days of menstruation from one cycle to the first day of menstruation in the next cycle.

The average duration of a normal menstrual cycle is between 25-30 days ²³. Menstruation cycles can be divided into two phases ^{1,23-25}:

(1) Follicular or proliferative phase, and (2) Luteal or secretory phase

(1) Follicular phase

The follicular phase starts from the first day of menstruation to ovulation. In this phase, estrogen levels in the blood increase by upregulation of receptor FSH (Follicle Stimulating Hormone). It affects the endometrium to rebuild and generate a new functional layer. The purpose of this phase is to increase the uterine endometrium layer. Besides, this step is also critical for creating an environment that is friendly and beneficial to potential incoming sperm. When this new layer grows bigger, its glands expand, and its spiral arteries increase in number. A primordial follicle starts to develop during this process to form a Graafian follicle that sets up for ovulation. Once the Graafian follicle is mature, the surrounding follicle begins to degenerate. Ovulation, which takes less than five minutes, occurs in the ovary in response to the release of LH (Luteinizing Hormone) from the anterior pituitary gland at the end of the proliferative stage. In this ovulation, the mature follicle releases the ovum. The ovum will then travel to the uterus where fertilization will take place.

(2) Fase Luteal (Sekretori)

This phase usually occurs for 14 days. During this phase, LHstimulated progesterone is the dominant hormone in preparing the corpus luteum and endometrium for possible fertilized ovum implantation. The corpus luteum is the transformation of the follicles that have released the ovum. Increasing progesterone levels from the corpus luteum cause the spiral arteries to develop and transform the functional layer into a secretory mucosa. The endometrial glands enlarge, coil, and begin to release nutrients into the uterine cavity that will support the growth of the embryo until it has been implanted into the endometrial lining that is rich in blood.

When progesterone rises, cervical mucus thickens and blocks the entry of sperm and pathogens or other foreign material. Increasing levels of progesterone (and estrogen) inhibit the release of LH by the anterior pituitary. If fertilization does not occur, the corpus luteum shrinks and signifies the end of the secretory phase as LH blood levels decreased. Estrogen and progesterone levels decrease, making the uterine lining eventually detached. The spiral arteries constrict one final last time and then suddenly relax and open wide. The detached tissue and blood pass out through the vagina called menstruation. This menstrual period usually occurs from zero to the fifth day. The follicular phase begins again to continue the process of the menstrual cycle.

Primary dysmenorrhea

Primary dysmenorrhea is characterized by lower abdominal cramps that can spread to the lower back and anterior or inner thighs. The painful cramps usually start a few hours before or during the early menstruation period and gradually decrease for two to three days. Sometimes, the cramps accompanied by nausea, vomiting, and diarrhea ⁶. Some risk factors associated with primary menstrual pain are menarche at an early age, family history with menstrual pain, abnormal body mass index, the habit of eating fast food, menstruation duration, cigarette, coffee consumption, and psychological symptoms such as depression and anxiety ^{6,7}. The etiology of primary dysmenorrhea is not yet fully understood. An imbalance of hormone-like prostaglandins probably causes the symptoms, thereby increasing uterine contractions that cause menstrual pain ^{21,26}. Prostaglandins are lipid autacoids derived from arachidonic acid that sustain homeostatic function and mediate pathogenic mechanisms, including the inflammatory response ²⁷. They are derived from arachidonic acid in the cyclooxygenase (COX) and lipoxygenase (LOX) pathways ^{27,28}. Prostaglandins help the uterus to contract and relax so that the thick layer formed at the luteal phase is released from the uterus. High levels of prostaglandins can cause stronger uterine contractions, and around 80% of patients can relieve the pain by using an inhibitor of prostaglandins. Research has shown that menstrual blood in women with primary dysmenorrhea has more PG - PGE2 and PGF2 α . Pain arises from myometrial contractions caused by PG (especially PGF2 α) originating from the secretory endometrium ²⁸. In addition, the existence of strong and longer duration of contractions in the uterine and the widening of the uterine during menstruation also causes primary dysmenorrhea ⁷. The lack of research in dysmenorrhea might be due to it is considered common and naturally occurred in women. Primary dysmenorrhea indicates that the pain is significant in chronic pain conditions that further research to relieve menstrual pain is needed.

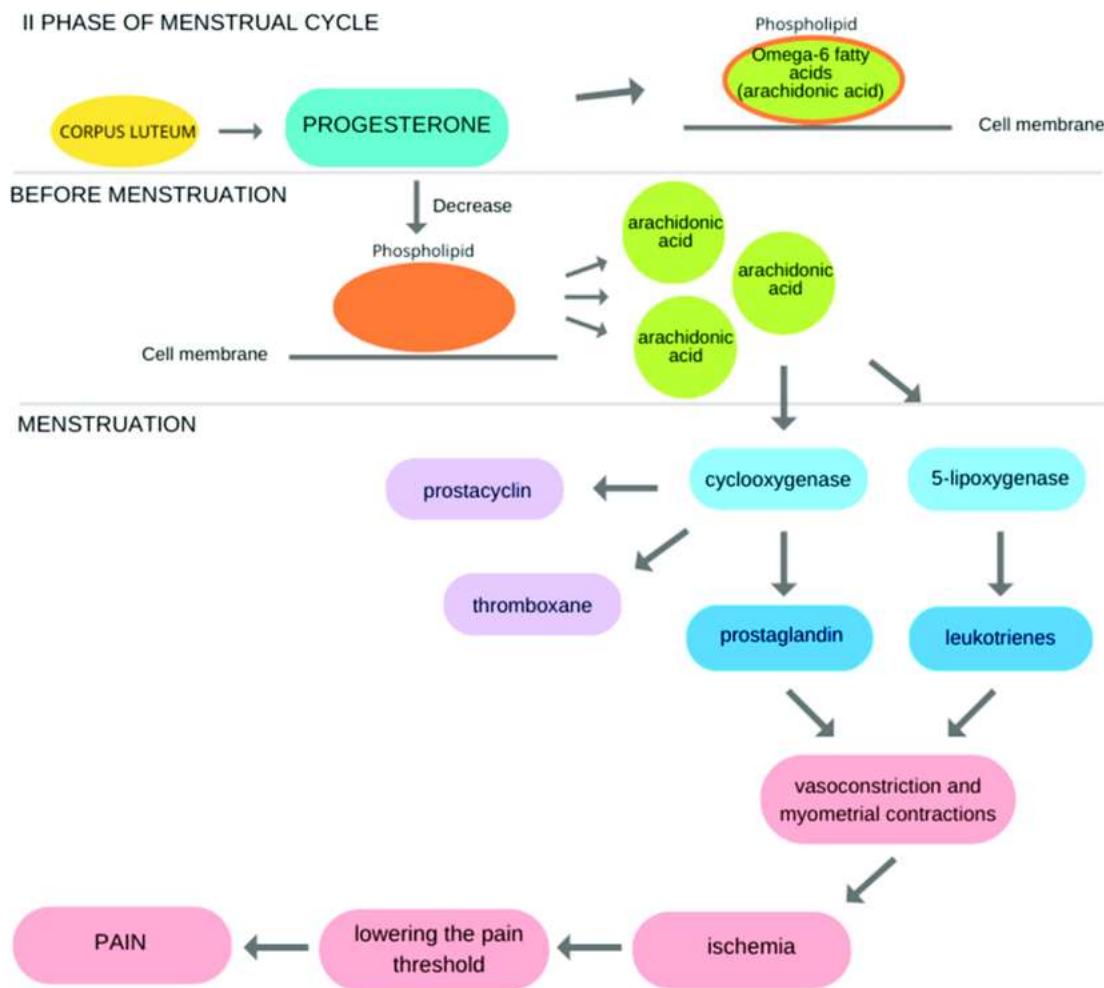


Figure 1: Possible mechanism of menstrual pain [29].

Curcumin

Curcumin or curcuminoid, a fat-soluble aromatic phyto-extract with orange-yellow pigment that has been firstly isolated from an Indian plant Turmeric (*Curcuma longa* L.) aromatic rhizome of the ginger family (Zingiberaceae) in 1870, and it is widely used as a food additive or natural coloring agent in Asia. The chemical structure of curcumin known as diferuloylmethane has been elucidated in 1910, the first study on its biological activity as an antibacterial agent according to the PubMed database has been published in 1949 Nature journal and the first clinical trial has been reported in 1937 Lancet journal. Until now, there are numerous in vitro, in vivo, and clinical studies that show it contained antioxidant, anti-inflammatory, anti-cancer, anti-diabetic, and anti-viral infection. The major constituents of curcuminoids contain Dihydrocurcumin, Tetrahydrocurcumin, Curcumin, Bis-demethoxycurcumin, and Demethoxycurcumin from turmeric (*C. longa* L.) rhizome. The beneficial health properties and medicinal values of curcumin include its effect on immune modulation, cardiovascular protection, and neuroprotection³⁰.

Curcumin and their benefits to reduce the menstrual pain

Research on the effect of curcumin on menstrual pain has been carried out³¹⁻³⁷. Research conducted in Indonesia mostly uses herbal medicine, which is processed using the main ingredients of curcumin and tamarind. This herbal medicine is believed to reduce primary dysmenorrhea. Several related studies also prove the effectiveness of herbal medicine. Curcumin has active ingredients that have function as

antioxidants, anti-inflammatory, and analgesics^{21, 38, 39}. Tamarind has active ingredients such antioxidants, antiinflammatory, antipyretic, and tranquilizers²¹. The effectiveness of herbal medicine has been proven by using statistical methods. All studies concluded that herbal medicine is very effective in reducing the level of pain of primary dysmenorrhea, and they recommend drinking herbal medicine before and during menstruation. Research conducted by Khayat et al. found that curcumin can also reduce the symptoms caused before menstruation and there are no temporary effects⁴⁰. Besides anti-inflammatory drugs, curcumin can also be used as an alternative to antidepressant drugs. A comparison of effectiveness among curcumin and other herbs was also carried out. Dyawapur et al. compared between cinnamon tea and curcumin. The study results that both cinnamon tea and curcumin have a significant effect on reducing menstrual pain⁴¹. Annugrahhayyu et al. conducted the effectiveness study between soy drinks and curcumin tamarind. The results indicate that curcumin tamarind reduces more menstrual pain than soy drinks³⁶. Sugiharti et al. also compared the effectiveness of curcumin tamarind with ginger tamarind. They found that both were effective in reducing the level of menstrual pain, but curcumin tamarind was slightly more effective in reducing primary menstrual pain³³. Besides for relieving menstrual pain, curcumin has many benefits. Research shows that curcumin helps in the oxidative and inflammatory conditions, metabolic syndrome, arthritis, anxiety, hyperlipidemia, improves recovery due to inflammation and muscle pain caused by exercise, and can provide other health benefits³⁸. Research on the effects of curcumin on tumor growth has also been conducted, and it was found that curcumin inhibits the process of angiogenesis

and metastasis on tumor growth³⁹. Curcumin could be used in the prevention or therapy of cardiovascular disease, respiratory diseases, cancer, neurodegeneration, infection,

and inflammation based on cellular biochemical, physiological regulation, infection suppression and immunomodulation.

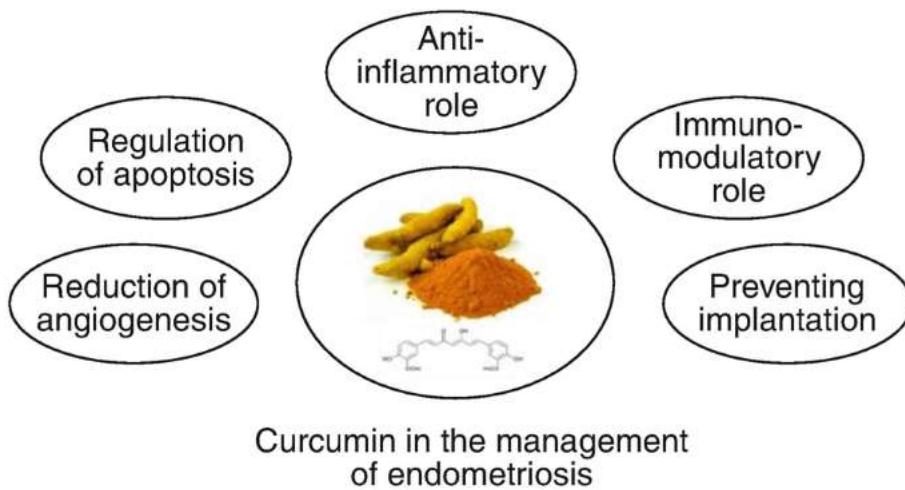


Figure 2: Curcumin in the management of endometriosis⁴².

Conclusion

Based on data from various researches relating to natural ingredients used in relieving primary menstrual pain, it was found that curcumin extract, which is usually mixed with tamarind and ginger is very effective in relieving primary menstrual pain. Several studies mention that menstrual pain caused by prostaglandin levels. Based on the literature, curcumin have an anti-inflammatory and antiprostaglandins effect of relieving primary menstrual pain. However, further research is needed to explore the etiology of primary dysmenorrhea more comprehensively. In addition, the mechanism of curcumin for relieving primary menstrual pain also needs to be explored.

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