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Alternative Treatments for Pain through Dhikr, Hijamah and Herbal Medicine as Integrative Medicine

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Abstract

Most people suffer pain at some stage of their lives. Therefore, pain is the most common reason to seeking therapeutic alternative or conventional medicine. Pain management particularly in chronic pain due to postoperative is systematically have been developed by various great recommendations that assist the health care practitioner and patient in making decisions about health care. In recent years, we have developed a better understanding of the pathomechanisms that link inflammation and peripheral sensitization about pain which can be overcome through an alternative treatment. This approach is known as complementary and alternative medicine (CAM). The development of the combined health approach has lately been known as Integrative Medicine, which seeks to restore and maintain health by understanding a series of patients' unique circumstances and overcoming their various physical, psychological, environmental, and spiritual influences. Through "whole system" treatment will be to elaborate an integrated approach, by dhikr, hijamah, and herbal medicine for facilitating the transition from viewing "pain" only as a matter of specific bodily functions (specific) to a more holistic view at the systemic level through integrative medicine to health care with a broader holistic approach.

Keywords: pain, integrative medicine, dhikr, hijamah, herbal medicine

1. Introduction

The term "alternative therapy" is generally used to describe any medical treatment or intervention that is used in place of conventional medicine. When alternative therapies are used in conjunction with conventional medicine, it is called complementary medicine. Alternative therapy covers a wide variety of disciplines. In the last decade, many evidences have been gathered for the benefits of mind-body therapy [1]. This approach has the potential to reduce pain in some cases. Mind-body therapy is a treatment intended to help the mind's ability to influence bodily functions and symptoms. Mind-body therapy uses a variety of approaches, including relaxation techniques, such as dhikr meditation, hijamah (wet cupping),

and herbal remedies approaches. These techniques can relieve the discomfort associated with chronic pain [2].

Pain is when the body's normal reaction to injury or illness, a warning that something is wrong. When the body heals, it usually stop getting sick. But for many people, pain persists long after the cause has gone away. If it lasts 3 to 6 months or more, it is called chronic pain [3]. When the body gets hurt day after day, it can affect the emotional and physical health. About 25% of people with chronic pain will continue to have a condition called chronic pain syndrome. That's when people have symptoms beyond just pain, such as depression and anxiety, which interfere with their daily life [3, 4].

Integrative medicine is defined as medicine that "reaffirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic and lifestyle approaches, healthcare professionals, and disciplines to achieve optimal health and healing" [5]. Integrative medicine incorporates all appropriate therapeutic approaches by all healthcare providers from both, conventional and complementary medicine, that are likely to improve an individual patient's health status [6, 7].

Integrative health care for pain management often brings together conventional and complementary approaches in a coordinated manner. It emphasizes a holistic patient-focused approach to health and wellness care - often covering mental, emotional, functional, spiritual, social, and community aspects - and treating as a whole bodily function. Thus, more research is needed to see how the complementary treatment for pain compares to conventional treatments [8, 9].

2. Dhikr meditation for pain management

Pain is a subjective experience involving biological, psychological, social and spiritual variables. Perceived pain is highly dependent on biological, psychological, social and spiritual variables [10]. One of non-pharmacological management method is meditation. It's focusing patient attention and easy to do anywhere, and does not require special equipment. Meditation is one of the most important non-pharmacological practices that promote relaxation. This is because through meditation, relaxation can provide an integrated response a psychophysiological response originating in the hypothalamus in the central nervous system [11, 12].

Meditation has physiological, mental, and spiritual benefits for the patients suffering from pain. In addition, meditation is an effective practice for pain management [13]. This can reduce the use of drugs or tranquilizers. Meditation is an activity undertaken to enter the state of unconsciousness and can strengthen soul, body, and mind and thus can reduce the sensation of pain. When someone meditates, the perception of pain can be minimized [14].

During practicing meditation, it was found that the brain produced large quantities of the pleasure-causing neuro-chemicals such as endorphins (as measured by EEG brainwave biofeedback machines) which made people a whole experience pleasurable, reduced pain, alleviated stress and gave an overall feeling of well-being. In addition, the alpha rhythm of the brainwaves was recorded during practicing meditation which led the patient to relaxation state [15]. The gate control theory for pain proposed by Melzack and Wall [16]. This theory explains the physical and psychological aspects of pain. It deals with nerve impulses that are released from every part of the body and modified in the spinal cord before being sent to the brain. It involves the spinal gate mechanism, central system, central biasing system, and action system. This correlative system works together rapidly when pain is felt [16, 17].

This theory proposes that the experience of pain is modulated by integrated emotional reactions, a relaxed state, and a meditative state in the higher centers of the brain (**Figure 1**), they modulate a noxipus input, reduces the perception of pain, and stimulates action to relieve it. Activation of the higher centers of the brain can cause the spinal cord gates to close. Closing the gate prevents pain input from reaching the higher centers of the brain, and translates into a total pain experience. The patient's reaction to pain includes the perception of pain intensity and physiological changes as a result of activation of the complex nervous system [17, 18].

To better understand this pain, a psychoneuroimmunological approach is used to explain the mechanism of acute pain, chronic pain and the working mechanism of pain control efforts including dhikr from the perspective of spiritual variables [19]. The mechanism of action of pain is not only played by the peripheral nervous system by involving neurotransmitters and cytokines, but also by the central nervous system [20]. The pain process from stimulation to perception, includes the role of modulation, where the modulation process occurs at the spinal level as well as at the brain level. At this modulation stage there are opportunities for therapeutic modalities, including dhikr, to control acute pain and chronic pain [21, 22].

Chronic pain mechanisms include the role of Long Term Potentiation (LTP), so that even though the cause of the pain is not found, the mechanism for generating pain stimulants can still occur, so that therapeutic modalities other than drugs are needed [23]; and from many research results show that the effectiveness of dhikr for controlling acute pain and chronic pain. Dhikr is one of the Islamic ritual forms, and used to concentrate the mind in order to experience calm inner feelings. Some of the research results of dhikr and the like which are effective in controlling pain and especially chronic pain, along with their biological mechanisms will be described in this section [24].

2.1 Dhikr through affirmation-tapping for pain management

Affirmation tapping interventions have been shown to reduce pain complaints in postoperative patients who have completed conventional treatment. This is thought to be due to serotonin's performance. The aim was to compare the mean perceived pain

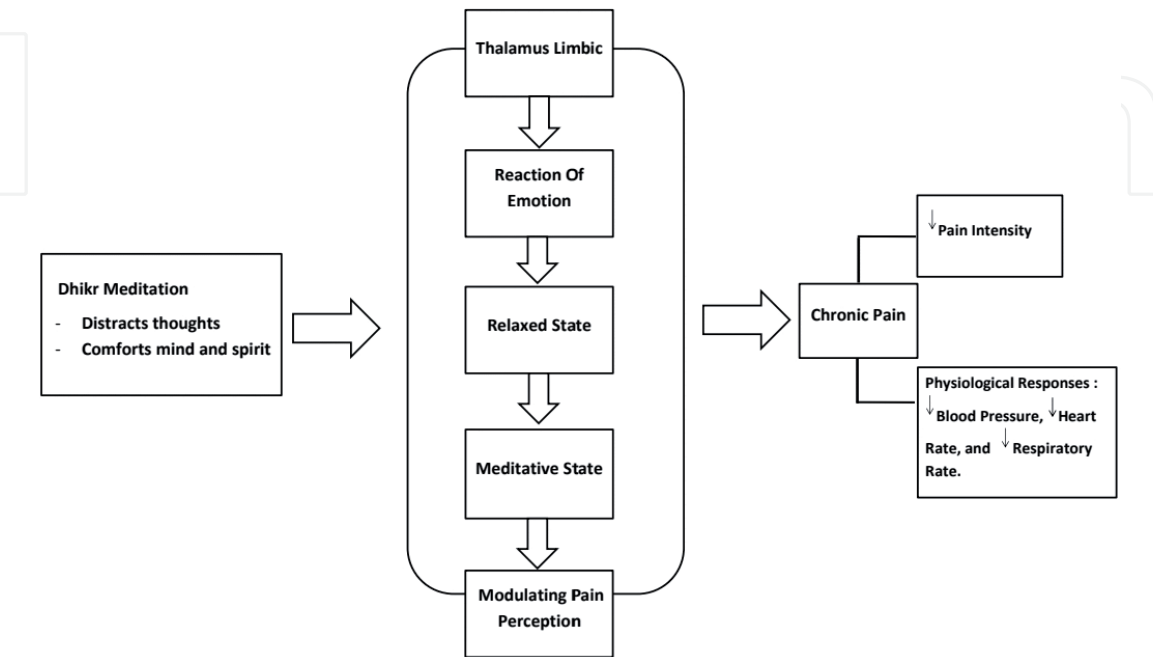


Figure 1.
Study framework effect of Dhikr for pain management among Muslim patients.

reported by postoperative patients who were given tapping treatment with the other treatments as complementary interventions. This study used a randomized post-test only control group design carried out in parallel with post-cesarean section patients. The sample consisted of 40 patients divided into four groups (10 in affirmation, 10 in tapping, 10 in affirmation-tapping and 10 in control). They were obtained through simple random sampling. The instruments include the tapping affirmation guide, the Elisa kit and McGill - Melzack Pain Questionnaire short-form (MPQsf) [25, 26]. The independent variable was affirmation-tapping intervention and the dependent variable was pain perception and serotonin levels. Data analysis included affirmation-tapping intervention, pain perception, and serotonin serum levels using simple linear regression. The Results showed the variation in the mean serotonin levels in the affirmation tapping treatment group was higher and significantly different from the other groups [26].

Therefore, affirmation-tapping as a complementary intervention can increase serum serotonin levels in post-cesarean patients by complementing conventional treatment. The lowest participant pain complaints were in the affirmation group with the highest serotonin levels and this differed significantly from the other groups [26]. Affirmation-tapping is recommended as a complementary intervention in postoperative patients that complements conventional medicine [26, 27].

Affirmation-tapping switches the activation of the pain process to inhibition of the pain process that occurs in the Pre Frontal Cortex (PFC) and Amygdala. In this state, through the performance of the descending pain modulator pathway, Peri Aqueductal Gray (PAG) modulated ON cells in the Rostral Ventromedial Medulla (RVM) to become inactive while the OFF cells in the RVM became active; and results in inhibition of the transmission of pain from the periphery to the central nervous system. The performance impact of PFC and PAG is supported by the perception of non-threatening, will stimulate peripheral inflammatory cells to secrete Serotonin, stimulate the secretion of Endorphins, which then modulate the transmission of pain in the Dorsal Horn spinal cord so that the perception of pain is not felt. Tapping on the acupoint will modulate peripheral inflammatory cells so as to reduce the secretion of IL6 and Glutamate, so that there is no inhibition of Serotonin and Endorphin secretion, and then inhibition of pain transmission in secondary neurons. Stimulation of Feishu (BL13), Hegu (L14), and Zusanli (ST36) accupoints resulted in lower interleukin-6 (IL6) and Glutamate [28]. Inhibition modulation in the Amygdala will increase the performance of the descendent pain inhibitor system through RVM and PAG so that pain transmission from the periphery in the spinothalamic pathway will be inhibited, so the overall pain perception is lower [26, 27, 29, 30].

2.2 Standard Operating Procedure for the implementation of affirmation-tapping

2.2.1 Affirmations

Affirmation of saying and or listening to and following the utterances of prayer, with a focused mind (only listening to and following prayer) and driven by the belief and hope that Allah will grant his prayers starting with istighfar 7 (seven) times, then ta'awudz and the Qur'an surah Al-Fatihah from verse 1 (one) to verse 7 (seven), slowly, the meaning is understood word for word. Prayers said and or heard, are repeated in the same order for up to 10 (ten) minutes [26].

2.2.2 Tapping

Tapping is performed by tapping the fingertips of another person's hand or tapping the tips of one's own fingers on acupuncture points. With a frequency of 2

(two) beats per second; With maximum power you can feel the beats, sequentially from GV 20 (Baihui), B1 (Tongziliao) right, BL 2 (Zanshu) right, B1 (Tongziliao) left, BL 2 (Zanshu) left, each 10 (ten) times and move; and back again starting from GV 20 (Baihui), and so on till time 5 (five) minutes [26].

2.2.3 Affirmation-tapping

Affirmation-tapping is done by saying or listening to and following the words of prayer, with a focused mind (only listening to and following prayer) and driven by the belief and hope of the fulfillment of prayer by Allah subhanallahu wa ta'ala, and coupled with tap the fingertips of another person or tap the tips of one's own fingers on acupuncture points. Prayers are said and or heard, repeated in the same order until 10 (ten) minutes, and at the 5th minute it is continued and added by tapping the tips of other people's fingers or tapping the tips of one's own fingers on acupuncture points, with a frequency of 2 (two) beats per second; with maximum power can be felt, sequentially from GV 20 (Baihui), B1 (Tongziliao) right, BL 2 (Zanshu) right, B1 (Tongziliao) left, BL 2 (Zanshu) left, each 10 (ten) times and moving; and back again starting from GV 20 (Baihui), and so on until a total time of 10 (ten) minutes [26].

2.3 Decreased pain perception through affirmation-tapping

Pain perception in all treatment groups was lower than the positive control group, and the lowest was found in the affirmation-tapping treatment group, which was accompanied by low levels of IL 6, Glutamate and high levels of Serotonin compared to the control group. The performance of brain in the pain process in the Pre Frontal Cortex (PFC), Amygdala can be modulated with the performance of the mind through affirmations, thereby increasing the performance of the decedent pain inhibition pathway, so that Serotonin secretion increases, and is still strengthened by tapping which results in decreased IL6 secretion which has an impact on decreasing glutamate secretion. and consequently the inhibition of Serotonin secretion is also reduced; thus Serotonin secretion is increased. The effect of serotonin on the decedent pain inhibition pathway is the release of endorphins which inhibit substance-P in the dorsal horn of the spinal cord, resulting in blockade of pain signal transduction to the brain. The Pain perception in all treatment groups was also lower than that of the positive control group. This is in line with Svensson's research, that IL-6 has a major influence in the induction and maintenance of pain as well as a regulator of emerging pathological pain [26, 27, 29, 30].

Decreased postoperative serum IL6 levels, reduced pain perception and reduced postoperative inflammatory response [30, 31]. Affirmation-tapping decreases pain perception more effectively than just affirmations, tapping and standard treatment. A process of awareness and focus of attention involves the performance of the pre frontal cortex (PFC) which will modulate the performance of the amygdala, resulting in adaptive performance. Research with experimental animals, it was found that the pain stimulation given would affect the performance of the amygdala, thus inhibiting the performance of PFC, where in the physiological condition, PFC could strengthen the performance of the Descendent-Pain Inhibition System so that the pain at the threshold value will not be felt [28].

A randomized controlled clinical study in a group of depressed women with Mindfulness exercise (which involved the performance of the Pre Frontal Cortex) and a control group with just a meeting, found that the Mindfullness group had lower levels of IL6 in saliva than the control group. This proves that the empowerment of PFC performance has an impact on reducing IL6 levels in the periphery.

The results of this study showed that in the Affirmation and Affirmation-tapping group, serum IL-6 levels were also lower than the control group. This finding is also supported by the results of a study in which groups specially trained in Mind Body Training also experienced decreased levels of IL6 [28].

Referring to the concept research model, affirmation-tapping, besides involving the performance of the Pre Frontal Cortex and Amygdala, also involves the performance of Inflammatory cells (Keratinocyte and Lymphocyte) so as to stimulate Pro-opiomelanocortin (POMC) to release endorphins, which are known to inhibit the transmission of pain signals [32]. Acupoint stimulation in Tapping treatment, can stimulate target cells so that it has an effect on modulation of target cell function in secreting certain cytokines. In experimental animal studies, with stimulation including the GV-20 acupoint (Bai Hui) which was also used in the Tapping treatment, it was found that a significant decrease in IL6 levels in plasma was found [33]. A study of Tu et al., also concluded that in a mouse model of depression with high glutamate and the acupuncture method was carried out, it could modulate glutamate to be low and the depressive effect due to high glutamate could be restored [34]. By extrapolating from these findings, it can be concluded that acupoint stimulation can make glutamate level was lower.

According to Garland's research, the "attention network" is one of the brain circuits most influenced by the practice of Affirmations. Accumulation of research suggests that affirmations are associated with beneficial neuroplastic changes in the "attention network" in particular, the Pre Frontal Cortex (PFC) and Anterior Cingulate Cortex (ACC) areas relevant to cognitive control, as a dimension of pain perception. Meta-analyses indicated that participation in affirmations was associated with greater activation and thickness of PFC and ACC. Change of broad neuroplastics in the "attention network" are associated with a number of specific results relevant to the construction of ongoing threats. For example, it was associated with increased dorsal activity of ACC during conflict detection and attention orientation. The Pre Frontal Cortex (PFC) and Anterior Cingulate Cortex (ACC) are involved in top-down regulation of negative emotional reactions to stressful and threatening stimuli used in the amygdala. Given the central role of the Amygdala in processing fear, anxiety, and negative emotions for the better and positive after affirmation, it is probably a function of the changes that are in the Amygdala. In affirmations that involve training activities to focus on the power and mercy of the Creator and emotional control have been repeatedly associated with wholesome structural and functional changes in the amygdala, including a decrease in gray matter and a decrease in the amygdala's response to negative emotional stimuli [35].

Furthermore, Affirmation transforms the functional connection between Amygdala and PFC in useful ways. Affirmative activity shows a significant reduction in resting functional connectivity of the Amygdala-subgenual ACC status which correlates with decreased biomarkers of chronic HPA axis activation, suggesting that affirmation can reduce molecular mediators of chronic stress by decreasing amygdala reactivity. This approach can be explained that affirmation-tapping, which combines prayer techniques and acupoint stimulation, works to reduce pain perception in two ways, namely increasing Serotonin by utilizing the performance of PFC, Amygdala, PAG, RVM and ITC (Descendent - Pain Inhibition System) as well. Reduced peripheral IL6 output and another way is to take advantage of the acupoint's performance so that it stimulates the POMC to release Endorphins and stimulates the Amygdala to free the Pre Frontal Cortex barrier to improve the performance of the Descendent-Pain Inhibition System [32–38].

3. Hijamah (wet cupping) for pain management

Traditionally, Cupping Therapy has been practiced and practiced in various cultures around the world. The Arabic name for cupping therapy is Al-Hijamah which means to reduce the size that is to return the body back to its original state. Al-Hijamah has been a part of Middle Eastern cultural practices for thousands of years (400 BC). From the western world, the first that perform cupping therapy was ancient Egypt, and the oldest medical recorded on a textbook, the Ebers Papyrus, was written since 1550 BC in Egypt. Anthropologists have also found evidence in China of cupping dating back to 1000 BC. Cupping has been known since ancient times, namely the Sumerian kingdom, then continued to expand to Babylon, Ancient Egypt, Saba, and Persia. At the time of the Prophet Muhammad, he used buffalo or cow horns, camel bones, elephant tusks [39].

Cupping is a simple technique of fast, strong, rhythmic movements to stimulate muscles and is very helpful in the treatment of aches and pains associated with various ailments. Thus, cupping has the potential to improve quality of life. There are two types of cupping. Dry cupping pulls the skin into the cup without bleeding. In wet cupping, the skin is torn off so that the blood enters the cup. The wet cupping technique (Al Hijamah) used in the Middle East is different from the technique used in Asia [40].

A hijamah application takes about 20 minutes and is done in five steps. The first step is primary desludging. In this phase, the therapist determines a specific point or area to be covered and then disinfects the area. The cup is sized according to the selected location and the therapist sucks the air inside the cup by manual suction technique. Then the cup is left on the surface of the skin and left for 3 to 5 minutes. The second step is about scarification or stabbing. A superficial incision is made into the skin using surgical knife No. 15 to 21, or pricking with a needle, or auto-lancing tool. The third step is suction and discharge of blood. The cup is placed back on the skin using the same procedure in the previous step and then left in the cup for 3 to 5 minutes. The forth step involves removing the cup, followed by the fifth step which involves drying the area from the blood and then attempting to clean it with a disinfectant. It can also be covered with a plaster strip on the scarified area for 1–2 days [41].

People get it for a variety of purposes, including to pain management, inflammation, stagnant of blood flow, relaxation, and deep tissue massage. Wet cupping therapy is becoming widespread and tends to be more prevalent in the Far East and in the Middle East and Eastern Europe. Wet cupping has been used as an alternative therapy in the management of patients with chronic pain [42]. However, high-quality trials are needed to produce stronger evidence.

Many published studies have shown that both techniques appear to be effective for patients with pain compared to an inactive control group but they were not compared in previous clinical studies. Wet cupping therapy also stimulates the inflammatory responses [43, 44]. The Middle East technique uses a three-step technique (a sequence of steps into cupping, stabbing, and cupping) in a continuous manner. General, where a sharp scalpel is used for scarification, and the nomenclature of the cupping place is also different. Asian techniques use a two-step technique. Cupping is applied only after piercing (piercing followed by cupping), which uses an automatic lancet needle rather than a scalpel. In certain countries or protocols they are guided by acupuncture points as cupping sites [45, 46].

The main difference is that in the Middle East, cupping is applied before and after skin scarification. Both techniques are currently used in cupping training programs in Saudi Arabia. However, traditional healers in Muslim countries prefer

local techniques such as those used during the time of the Prophet of Islam. Wet Cupping is indicated for blood disorders, pain relief, inflammatory conditions, mental and physical relaxation, tissue massage. Cupping is done to extract blood believed to be harmful from the body which in turn removes the potential harm from the body's symptoms leading to health problems [47]. The main goals of this therapy are to accelerate blood circulation and to remove blood-stasis and waste from the body [48]. Benefits of cupping by creating a suction through negative pressure on the surface of the skin is known to affect body up to four inches into the tissue. Cupping can also be used to treat muscle pain and spasms, draining away excess fluids and toxins, loosens adhesions, connective tissue and hard knots in soft tissue, stimulates circulation and promotes stagnant blood flow to muscle tissue and skin, thereby increasing energy flow, stimulates the peripheral nervous system, and activates the lymphatic flow system (**Figure 2**) [40, 47].

The mechanism of wet cupping therapy (Al Hijamah) is started from the clogged blood that will be removed from the skin, thereby improving blood and lymphatic circulation and relieving painful muscle spasms, and this will have the desired effect. Wet cupping can cause the production of endogenous nitric oxide (which is considered a vasodilator) or removes oxidants, which reduces oxidative stress. In addition, lacerations of the skin can induce pervasive inhibitory control, which in turn acts as a nociceptive stimulus. The mechanism has been explained by Pain-Gate Theory (PGT).

This theory is one of the most influential theories on pain reduction introduced by Melzack and Wall since 1965 [49]. They explain that injuries due to touch, pressure, and vibration to the surface of the skin carry pain signals from the site of injury to two destinations in the dorsal marrow, the spine, and transmitting pain signals to the brain. While interneurons work as an inhibitor of cell transmission activity. The theory comprehensively explains how pain is transmitted from the point of origin of pain to the brain, and how it is processed in the brain, then sends signals back to the injured efferent area. The wound inflicts local damage to the skin and capillaries acting as a nociceptive stimulus. This Theory was origin from the neuronal hypothesis that cupping can treat chronic pain by altering signal delivery at the level of nociceptors in both the spinal cord and brain [49].

The clinical manifestations of cupping in a randomized control trial report that cupping can be an effective therapy for pain management. The activity in thin and large diameter fibers supports the work of the transmission cell. Thin fiber activity inhibits interneuron cells (tends to allow transmission cells) and large diameter

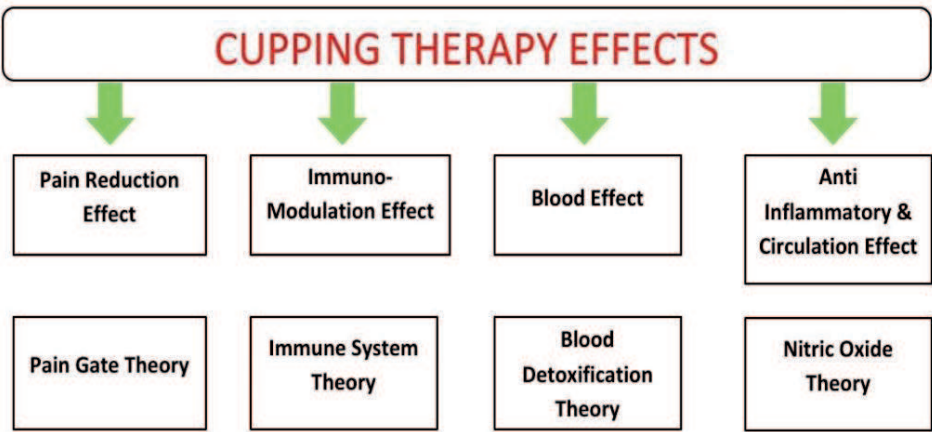


Figure 2.
Possible mechanism of cupping action theories.

fiber activity stimulates interneuron cells (tends to inhibit transmission cell activity). It can be concluded that the greater the activity of touch, pressure, and vibration on the skin surface, the less pain is felt. Thus, it is hoped that activation of nociceptors through cupping can stimulate “A” and “C” fibers with the involvement of the spino-thalamo-cortical pain pathway. The peripheral nociceptors can be sensitized by metabolic factors such as lactate, adenosine triphosphate, and cytokines. When a stimulus is applied to the surface of the skin, it increases the number of fiber-receptor units that are active to receive the stimulus that will be transmitted to the brain. Cupping therapy can reduce pain through its anti-nociceptive effects by fighting irritation. So it is believed that cupping therapy stimulates pain receptors by increasing the frequency of impulses, which in turn closes the pain gate [49].

4. Herbal Medicine for Pain Management

4.1 Cytokine, inflammation and pain

Cytokines are small amounts of proteins that mediate the relationship between cells, cytokines are the link between immune cells and nerve cells. Cytokines play a role in the process of immunity, inflammation and hematopoiesis. Both pro-inflammatory and anti-inflammatory cytokines are involved in pain process. There is significant evidence that certain cytokines are involved in not only the initiation but also the persistence of pathologic pain by directly activating nociceptive sensory neurons. Based on its effect on immune cells, especially lymphocytes, cytokines are divided into 2, namely pro-inflammatory cytokines, including: $\text{TNF } \alpha$, $\text{IL-1}\beta$ (Interleukin) and IL-6 and anti-inflammatory cytokines, including: IL-4 and IL-10 . Pro-inflammatory cytokines have algescic properties whereas anti-inflammatory cytokines are analgesic. Pro-inflammatory cytokines are produced in the early phase while anti-inflammatory cytokines in the late phase of inflammation [50].

The three pro-inflammatory cytokines can each induce production of one another and work synergistically. Meanwhile, anti-inflammatory cytokines suppress the gene encoding IL-1 , $\text{TNF } \alpha$ and chemokine. A research in the role of cytokines in the pathogenesis of pain has been extensively investigated. In animal models, peripheral nerve lesions will immediately be followed by changes in cytokine expression continuously where cytokine levels increase in both the peripheral and central nervous system. A study proposed the Law of Pain hypothesis which states that all pain originates from inflammation and inflammatory responses, regardless of whether the pain is acute or chronic, peripheral or central and nociceptive or neuropathic pain [50, 51].

Neutrophils and macrophages both produce and secrete inflammatory mediators such as $\text{TNF-}\alpha$, Prostaglandin E_2 (PGE_2), bradykinin, serotonin, histamine and so on. These inflammatory mediators directly activate nociceptors or cause sensitization of nociceptors, causing both spontaneous inflammatory pain and primary hyperalgesia. Neural lesions also cause Schwann cells to de-differentiate and release several algescic mediators such as: pro-inflammatory cytokines [50].

There is also the recruitment of T lymphocytes which can secrete various cytokines depending on the subtypes. These mediator cytokines play a role in the inflammatory response due to primary afferent nerve lesions and contribute to neuropathic pain. A study also explained that the cytokines Interferon-gamma ($\text{IFN-}\gamma$) can induce hyperexcitability of dorsal horn neurons in vitro, suggesting that pro-inflammatory cytokines play a role in central sensitization [50, 51].

4.2 Natural compounds for inflammation therapy and pain management

Pain is a nociceptive sensation in which perception causes unpleasant emotions. It is accepted that sensitization of primary sensory neurons is essential for inflammatory pain. Nonetheless, this nociceptor sensitization was, for a long time, thought to be the result of the stimulatory action of various inflammatory mediators i.e. cytokine released at the site of inflamed or damaged tissue. Cytokines generally function as intermediate mediators, releasing other cytokines and end mediators. In some cases, however, cytokines can act as late hyperalgesic mediators and several studies have described the involvement of cytokines in the development of nerve cell damage that will contribute to the onset of pain symptoms that are felt differently than expected by the type of stimulus applied (touch, for example, can produce stabbing pain). In one review, an expression used the term “hyper-nociception” to describe increased pain sensitivity by primary nociceptor neurons in an animal model [52]. Both in vitro and in vivo clinical evidence showed that cytokines play an important role in the mechanism of neuropathic pain can guide alternative therapeutic strategies that target humoral signal molecules and provide opportunities for the development of herbal drugs that can prevent or treat neuropathic pain. There have been studies explaining the evidence supporting the role of cytokines in pain manifestation. It discusses possible therapeutic approaches for pain control using therapies that target cytokines such as dissolved receptors, receptor antagonists, neutralizing antibodies, as well as herbal therapeutic approaches aimed at inhibiting cytokine production [53].

Many significant side effects of taking steroids and nonsteroidal anti-inflammatory drugs (NSAIDs) have led to greater interest in natural compounds, as dietary supplements and as herbal remedies, which have been used for centuries to reduce pain and inflammation. Natural compounds derived from plants and animals have been used for hundreds or even thousands of years to find effective pain relievers. Herbal medicine is becoming popular because of its relatively few side effects. However their use still requires knowledge of their biological action, clinical studies and potential interactions with other prescription drug products. Many researchers will reinforce the positive findings on the use of natural compounds to treat diseases, including pain management [54].

Recently, several herbal studies have shown that blends in various extracts from various herbs are predicted to be more effective than a single purified natural ingredient. A new study reports on the potential for polyherbal extracts to reduce inflammation. The novelty polyherbal used in this study is EMSA ERITIN. EMSA ERITIN contains soybeans, brown rice and coconut water. The EMSA ERITIN polyherbal composition has been shown to be effective in suppressing inflammatory transcription factors. EMSA ERITIN consists of soybean extract [53], coconut water extract [54] and brown rice extract. As we know soybeans contain many active compounds. One of the active compounds is genistein. Genistein is an isoflavone isolated from soy, is a powerful antioxidant with good anti-inflammatory effects. The results of this study indicate the effect of poly-herbal EMSA ERITIN can suppress pro inflammatory cytokines, TNF- α and IFN- γ in vivo. The study also looked at transcription expression of inflammatory factor (NF- κ B). EMSA ERITIN exhibits anti-inflammatory activity when administered to lymphocytes in BALB/c mice after radiation [55]. EMSA ERITIN can decrease proinflammatory cytokine TNF- α and IFN- γ , also transcription factor of NF- κ B. The increasing of dose in EMSA ERITIN showed more effective than lower doses. So, EMSA ERITIN is potential polyherbal plant used as anti-inflammatory agent [55] and further it can be studied for used as herbal medicine for pain relief.

The hypothesis that all pain processes originate from inflammation and inflammatory responses, as well as the hypothesis that pain occurs due to an imbalance between pro and anti-inflammatory cytokines needs to be studied more deeply,

so that if the hypothesis is proven correct, thus the therapeutic strategy can inhibit pro-inflammatory cytokines. or increasing anti-inflammatory cytokines would hopefully have more promising results.

5. Conclusion

Complementary and alternative medicine has grown in the past decades with many of its systems worldwide. Integrative approaches in pain control methods for Muslims patients in addition to: preventing cell damage, reducing the effect of chemical mediators of pain can be managed by dhikr, hijamah and herbal medicine. It was recommended that dhikr therapy through affirmation-tapping either singly or in combination with hijamah and herbal medicine can significantly reduce pain intensity. Cupping therapy (Al hijamah) was cited by Muhammad (PBUH), Wet cupping (Al-hijamah) is a therapeutic approach that is believed to combat illness and promote well-being. Also the herbal medicine for healing purposes predates human history and forms the origin of much modern medicine. These approaches will be a promise therapeutic as integrative care for pain management.

Acknowledgements

We are grateful to Prof. Drs. Sutiman B. Sumitro, DSc for his valuable guiding in the complexity sciences.

Conflict of interest

The authors declare no conflict of interest.

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