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# Are Topical Heat Patches More Effective at Relieving Pain Associated With Dysmenorrhea Than OTC NSAIDs (Ibuprofen 400 mg PO Q8h or Acetaminophen 500 mg PO Q6h) in Menstruating Women 18 and Over?

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Abstract

Objective: The objective of this selective EBM review is to determine whether or not topical heat patches are more effective at relieving pain associated with dysmenorrhea than OTC NSAIDs (Ibuprofen 400 mg PO Q8h or Acetaminophen 500mg PO Q6h) in menstruating women 18 and over.

Study Design: Review of three English-language randomized control trials (RCTs) that were published in 2001, 2004, and 2012.

Data Sources: Three single-blinded randomized control trials that were found using PubMed

Outcome measured: Dysmenorrhea and any associated pain relief was measured using patient-reported scales of NRS-10 Pain scale, 6-Point categorical scale, and patient reports of sensual, emotional, current, and total pain.

Results: Akin et. al 2001 and 2004 studies found that topical heat patches were associated with statistically significant greater reduction in pain associated with dysmenorrhea than oral NSAIDs. A 2012 study by Navvabi Rigi, et al., however, showed no statistically significant difference in pain reduction in patients that received topical heat versus an oral NSAID.

Conclusions: Some studies have shown that topical heat causes greater pain reduction than oral NSAIDs, though the results are inconclusive among all studies. Further studies with larger sample sizes and double blinding will be needed to determine the true effectiveness of topical heat in treating pain associated with dysmenorrhea versus oral NSAIDs.

Key Words: Heat, dysmenorrhea

## INTRODUCTION

Dysmenorrhea is pain associated with a woman's menstrual cycle that is believed to occur as a result of necrosis of the endometrial layer[3]. This paper evaluates 3 RCTs that compare the efficacy of topical heat patches as a treatment for dysmenorrhea against traditional OTC NSAIDs.

Dysmenorrhea is a very common problem affecting an estimated 15.8 – 89.5% of women of childbearing age worldwide[3]. Rates of dysmenorrhea are higher among adolescents, with prevalence and severity generally decreasing with age[3]. Since painful menstrual cramps are such a common problem, it is no surprise that dysmenorrhea is a leading cause of absenteeism from work and is the most common reason for school absence in young women[4]. In addition to causing a disruption in women's education and work, dysmenorrhea takes a toll on the health care system. It is estimated that 14-18% of young women with primary dysmenorrhea seek primary care[2].

Primary dysmenorrhea is believed to be caused by the myometrial stimulant and vasoconstrictor, prostaglandin F2α (PGF2α)[4]. Traditional methods of treatment have included oral contraceptives; prescription and over the counter nonsteroidal anti-inflammatory drugs such as Diclofenac, Ibuprofen, Ketoprofen, mecloenamate, and naproxen; dietary supplements such as thiamine, fish oil, pyridoxine, magnesium, and vitamin E; Exercise, and acupuncture[4]. In addition to these remedies, however, topical heat has long been a home remedy for treatment of dysmenorrhea via hot water bottles and electric heating pads. These methods, however, are impractical for use throughout the day. With the creation of topical heat pads, it will be beneficial to compare their efficacy against OTC NSAIDs in the treatment of dysmenorrhea due to the side effects of chronic NSAID use[2]. The traditional treatment, OTC NSAIDs are also

known to cause GI inflammation, bleeding, rash, pruritis, tinnitus, dizziness, and renal or hepatic complications, making the prospect of using topical heat even more appealing[3].

**OBJECTIVE**

The objective of this selective EBM review is to determine whether or not topical heat patches are more effective at relieving pain associated with dysmenorrhea than OTC NSAIDs (Ibuprofen 400 mg PO Q8h or Acetaminophen 500mg PO Q6h) in menstruating women 18 and over.

**METHODS**

Specific selection criteria of three randomized control trials (RCTs) were used for this review. The population studied was made of menstruating women, aged 18 and over, with a history of dysmenorrhea. In each of the 3 RCTs a topical heat patch was used as the intervention. Additionally, each RCT compared the pain relief provided by the heat patch against an OTC NSAID - either Ibuprofen 400 mg Q8hr or Acetaminophen 500 mg PO Q6h. The outcome measured in each of the RCTs was a decrease in symptoms of dysmenorrhea and any associated pain relief.

The studies included in this review were three randomized control trials (RCTs). Keyword searches to obtain these articles included the words “heat” and “dysmenorrhea”. Each of the articles was published in peer-reviewed journals in English. RCTs for this review were searched for by the author of this review via PubMed and were selected based on their relevance to the clinical question and patient-oriented outcome. Inclusion criteria included studies that were randomized control trials published between 1999 and the present. Studies were excluded if they were published before 1999 or included patients less than 18 years of age. Statistics included in these 3 RCTS included mean change in pain from baseline, p values, odds ratios, and number needed to treat. Table 1 shows the demographics of the included studies.

**Table 1: Demographics of Included Studies**

| Study | Type | # Pts | Age (years) | Inclusion Criteria | Exclusion Criteria | W/D | Interventions |
|---|---|---|---|---|---|---|---|
| Akin, 2001 (1) | RCT | 84 | 21-50 | Patients that are non-pregnant women of menstrual age who suffer from moderate or severe menstrual pain for at least 4 of their last 6 menstrual cycles, at least 18 years of age, have a hx of pain relief from OTC analgesics and use reliable forms of contraception | Patients that use any other supplemental devices or analgesics during the period of the study, engage in vigorous exercise, excessive alcohol consumption, or sexual intercourse during the 12 hours before the study and throughout the remainder of the study, patients with cutaneous lesions involving the abdominal wall, microvascular disease, known/suspected drug or alcohol abuse, known/suspected contraindication to oral ibuprofen, and patients that are pregnant or recently pregnant | 3 | Topical heat abdominal patches and placebo pill VS Placebo patch and 400 mg ibuprofen PO Q6hrs |
| Akin, 2004 (2) | RCT | 367 | 18-50 | Patients that are premenopausal women at least 18 years of age with a medical history, physical, and pelvic exam consistent with primary dysmenorrhea, women must also have regular, monthly periods over the last 9 months with moderate or greater menstrual pain occurring in at least 4 of their last 6 menstrual cycles as well as a consistent use of contraception | Patients with known contraindication to use of study medication or devices, history positive for secondary dysmenorrhea, use of hormonal contraceptives of IU for < 6 months, consistent use of medication that could interact with the study medication, devices, or evaluation parameters | 23 | Continuous, low-level, topical heat wrap VS. Acetaminophen 500mg PO Q6Hrs |
| Nawabi Rigi, 2012 (3) | RCT | 147 | 18-30 | Patients aged 18-30 with a hx of dysmenorrhea within the first 2 years of onset of menstruation with regular menstrual cycles, good general health and a hx of moderate to severe dysmenorrhea | Patients with a hx of comorbidities (including cardiovascular, renal, hepatic, pulmonary), coagulopathy, DM, anemia, GI bleeding, immunological disorder, malignancy, psychiatric illness requiring therapeutic intervention. Also, patients with a hx of oral contraceptives, smoking, pregnancy, professional athlete activity, lower abdominal scars, BMI > 30, and vagnitis, or recent death or stress in the family | 42 | Iron chip-containing heat wrap VS Ibuprofen 400mg PO Q8hr PRN |

## OUTCOMES MEASURED

Each of the three RCTs used patient-reported pain scales in order to determine the effectiveness of the topical heat patch versus the NSAID. The studies, however, varied in methods of rating patient-reported pain. Since the patients could not be blinded to which treatment they were receiving, each of the studies was single-blinded – meaning the individuals recording data for the study were not aware to which group each patient belonged. The two studies by Akin M, et. al used both the 6 point categorical scale and the NRS-101 to record patient pain[1,2]. The 6-point categorical scales ranges from zero to five – zero representing no pain, while five indicates maximum pain[1,2]. The NRS-101 scales ranges from zero to one hundred – zero representing "not unpleasant at all" and one hundred representing "the most unpleasant feeling possible for me."[1,2] The 2012 study by Navvabi Rigi, et. al used the short form of the McGill Pain Questionnaire, also known as the SF-MPQ, to measure pain. SF-MPQ consists of 15 descriptors[3]. It has been proven to be a reliable tool with proven validity in assessing obstetric patients and has been previously used to assess dysmenorrhea[3]. Additionally, the 2012 study used visual analog scales ranging from zero to one hundred to rate current pain and from zero to five to rate "overall pain severity"[3].

## RESULTS

The 2001 study by Akin et. al was a randomized, placebo and active control "double dummy", parallel study[1]. Eighty-four women were found to be eligible for the study, with eighty one of them completing it[1]. The three women who did not complete the study were lost due to their failure to follow study protocol – "worst case" analysis was not performed[1]. Inclusion criteria for this study included non-pregnant women of menstrual age who suffered from moderate to severe menstrual pain for at least the last 4 of their 6 menstrual cycles; at least 18 years of age; history

and physical consistent with primary dysmenorrhea; have a history of pain relief from OTC analgesics; reliable contraception including barrier, abstinence, or sterilization[1]. Exclusion criteria for this study included use of any supplemental devices or analgesics during the study period; vigorous exercise, alcohol consumption, or sexual intercourse during the 12 hours before the study and throughout the remainder of the study; cutaneous lesions of the abdominal wall; microvascular disease including diabetes; known or suspected drug or alcohol abuse; known or suspected contraindication to oral ibuprofen; pregnant or recently pregnant[1]. Women were randomly assigned to one of four groups using a computer program[1]. The four groups were as follows - heated patch plus ibuprofen, heated patch plus placebo, unheated patch plus ibuprofen, and unheated patch plus placebo[1]. Women were given "kidney bean-shaped ultra-thin medical devices" to adhere to the inside of their underwear on the lower abdominal region which was standardized between participants[1]. The patches supply constant heat of 38.9°C for 12 hours, after which it was replaced with a new one[1]. Women assigned to ibuprofen groups were given 400 mg ibuprofen three times a day, six hours apart[1]. This review is focused on the results of two groups – unheated patch plus ibuprofen (n=21) and heated patch plus placebo (n=20) [1]. Pain relief was recorded every two hours for two days. During the 2 day study, women receiving the unheated patch plus placebo had a 35% incidence of complete pain reduction[1]. Women who received the experimental treatment of heated patch plus placebo had a statistically significant incidence of complete pain relief of 70%, OR 4.3%, $p = 0.015$ (Table 2) [1]. Women assigned to the unheated patch and ibuprofen group, however, did not have a statistically significant incidence of complete pain relief at only 55%, OR 2.3, $p = 0.103$ (Table 2) [1]. These numbers correlate to a relative benefit increase (RBI) of 0.273, an absolute benefit increase (ABI) of 0.150, and a number needed to treat (NNT) of 7 (Table 3). This study shows that the use of heat

patches alone for treatment of pain associated with dysmenorrhea is statistically significantly better than placebo while the use of the traditional use of ibuprofen alone is not. The study showed that for every 7 people treated with the heat patch plus placebo, one had more pain relief than those treated with the unheated patch plus ibuprofen. Factors that may have affected the study include redness at the adhesion site of the patch as well as other symptoms of dysmenorrhea including breast fullness and tenderness.

**Table 2: 2001 Akin Study: Unheated Patch plus Ibuprofen vs. Heated Patch plus Placebo**

| | **Placebo** | **Control** | **Experimental** |
|---|---|---|---|
| **Treatment** | **unheated patch plus placebo** | **unheated patch plus Ibuprofen** | **heated patch plus placebo** |
| Number of patients, N | 20 | 21 | 20 |
| Incidence of complete pain relief at day 2 | 35% | 55% | 70% |
| Odds Ratio, OD | --- | 2.3 | 4.3 |
| p value | --- | 0.103 | 0.015 |

**Table 3: 2001 Akin Study: Statistical Analysis of Heated Patch plus Placebo vs. Unheated Patch plus Ibuprofen**

| **CER: unheated patch plus ibuprofen** | **EER: heated patch plus placebo** | **Relative Benefit Increase, RBI** | **Absolute Benefit Increase, ABI** | **Number needed to treat, NNT** |
|---|---|---|---|---|
| 0.55 | 0.70 | 0.273 | 0.15 | 7 |

The 2004 study by Akin et. was a randomized, active control, parallel, single-blind, multisite study[2]. Three hundred sixty seven women were entered into the initial study with three hundred forty four women completing the study[2]. Patients were lost due to violations related to dosing compliance as well as study drop out – "worst case" analysis was not performed[2]. Inclusion criteria for the study included premenopausal women of at least 18 years of age; a medical history, physical, and pelvic exam consistent with primary dysmenorrhea; women that had

regular, monthly periods over the last 9 months with moderate to severe menstrual pain occurring in at least 4 of their last 6 menstrual cycles; consistent use of contraception; and absences of a history of secondary dysmenorrhea[2]. Exclusion criteria for the study included known contraindication to use of the study medications or devices; use of hormonal contraception or IUD for less than 6 months; consistent use of medication that could interact with the study medication, devices, or evaluation perameters[2]. Women were randomized to one of four groups – oral acetaminophen (n = 156), active heat wrap therapy (n = 155), oral placebo (n = 22), and inactive heat wrap (n = 24). The mean age of the women enrolled in the study was 28.8 years old[2]. Oral acetaminophen dosing was 500 mg twice a day, 8 hours apart[2]. Participants were randomly assigned and groups were equally random based on race, daily tobacco use, age, height, and baseline pain intensity[2]. The study measured pain relief using a 6 point categorical scale at hours 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 24, and 48[2]. This study showed that at the end point of day 1, the heat wrap group had a statistically significant mean pain relief score (2.48 ± 0.10) compared to the oral acetaminophen group (2.17 ± 0.10, p value = 0.015) seen in Table 4[2]. This indicates that at the end of the first 8 hour day, the heat wrap group had significantly less pain than the acetaminophen group. Additionally, the heat wrap group reported less adverse events compared the acetaminophen group, 2 versus 4, respectively (Table 5). The two adverse events in the heat wrap group were a mild conjunctivitis and moderate application site reaction[2]. The four adverse events in the acetaminophen group were moderate head ache, moderate rhinitis, moderate respiratory infection, and severe anxiety[2].

**Table 4: 2004 Akin Study: Acetaminophen vs. Heat Wrap**

| | **Control** | **Experimental** |
|---|---|---|
| **Treatment** | **Acetaminophen** | **Heat Wrap** |
| Mean pain relief from baseline | 2.17 | 2.48 |
| standard deviation | 0.1 | 0.1 |
| p value | 0.015 | |

**Table 5: 2004 Akin Study: Adverse Events**

| **Control** | **Experimental** |
|---|---|
| **Acetaminophen** | **Heat Wrap** |
| moderate Head ache | mild conjunctivitis |
| moderate rhinitis | moderate application site reaction |
| moderate respiratory infection | --- |
| severe anxiety | --- |

The 2012 study by Navvabi Rigi, et. al was a randomized control trial with blind raters[3]. 186 women were assessed for eligibility in the study with 39 women being excluded for not meeting inclusion criteria[3]. Inclusion criteria included age 18-30, history of dysmenorrhea within the first 2 years of onset of menstruation, regular menstrual cycles, "good" general health, and a history of moderate to severe dysmenorrhea[3]. Exclusion criteria for this study included history of cardiovascular, renal, hepatic or pulmonary comorbidities; history of oral contraceptives, smoking, pregnancy, professional athlete activity, lower abdominal scars, BMI > 30, vaginits, or recent death or stress in the family[3]. The remaining 150 women were randomly assigned to one of two groups – ibuprofen ( n = 75) and heat patch ( n = 75) [3]. Three women of the heat patch group were lost because they did not receive the allocated intervention – worst case analysis was not performed[3]. There were no statistically significant differences among the two groups in respect to marital status, socio-economic status, BMI, or abdominal circumference[3]. The dose of ibuprofen given to the women in the ibuprofen group was 400mg by mouth every 8 hours as

needed for pain[3]. In this study, current severity of pain was measured on a 0-100 scale by patients. This study shows that when "current pain" was measured at hour 8 of treatment, the ibuprofen group had a slightly lower, though statistically insignificant, total pain score – indicating a T score of 1.18 and a p-value of 0.24 (Table 6) [3]. The authors found it important to note that the maximum effectiveness of the heat patch is 8 hours. It is also important to note that only 79% of the initial participants were eligible and completed the study[3].

**Table 6: 2012 Navvabi Rigi Study: Student T Test comparing Ibuprofen vs. Heat Patch**

| | |
|---|---|
| **T Test** | 1.18 |
| **P Value** | 0.24 |

## DISCUSSION

This systematic review used three randomized control trials to assess the effectiveness of topical heat in pain relief associated with dysmenorrhea compared to oral non-steroidal anti-inflammatory drugs. Two of the three studies included in this review showed significantly greater pain relief when using topical heat as compared to oral NSAIDs[1,2]. One study, however, showed no statistical significantly difference between the two treatments when measuring total current pain at hour 8[3]. It is important to note however, that these studies had some limitations.

The 2001 Akin et. al study included only 84 women, which is not expected to accurately represent an entire population[1]. Furthermore, the 2004 Akin et. al study and the 2012 Navvabi Rigi study only had 367 and 147 women total in each of their studies, respectively[2,3]. The other limitation of these studies is that none of the studies were double-blinded. Participants would be aware if they were only being treated with a heat patch vs. pill[3] or a heated vs. unheated patch[1,2] which made double-blinding difficult. It is also important to note that prior studies have showed that pharmacotherapy is general ineffective in treating dysmenorrhea in 20-25% of the

population[3]. Also, since these RCTs studied pain, it is important to remember that individuals have varying pain tolerances and this was not accounted for during randomization in each of the three studies. Lastly, it is also important to remember that two of the three studied ibuprofen as the oral NSAID of choice, while one used acetaminophen. Additionally, all three studies used different dosing of the oral NSAIDs which could have resulted in different results among the studies.

**CONCLUSIONS**

The purpose of this systematic review is to determine whether or not topical heat patches are more effective at relieving pain associated with dysmenorrhea than OTC NSAIDs (Ibuprofen 400 mg PO Q8h or Acetaminophen 500mg PO Q6h) in menstruating women 18 and over. The results of the three randomized control trials are inconclusive. The two studies performed by Akin et. al showed that patients treated with topical heat patches have statistically significant greater pain reduction that those taking oral NSAIDs[1,2]. A study by Navvabi Rigi et. al, however, showed no statistically significant difference in pain relief between patient using topical heat patches versus oral NSAID[3].

Due to the high prevalence of dysmenorrhea[3], low incidence of adverse event of using topical heat patches[2] and relatively low cost of heat patches[3], it would be advantageous to continue with further studies on this topic. Further studies should work to blind participants, include larger sample sizes, and take pain tolerance into account when randomization the sample.

REFERENCES


1. Akin MD, Weingand KW, Hengehold DA, Goodale MB, Hinkle RT, Smith RP. Continuous low-level topical heat in the treatment of dysmenorrhea. *Obstet Gynecol*. 2001; 97(3):343-9.

2. Akin M, Price W, Rodriguez G, Erasala G, Hurley G, Smith RP. Continuous, low-level, topical heat wrap therapy as compared to acetaminophen for primary dysmenorrhea. *J Reprod Med*. 2004;49(9):739-45.

3. Navvabi rigi S, Kermansaravi F, Navidian A, et al. Comparing the analgesic effect of heat patch containing iron chip and ibuprofen for primary dysmenorrhea: a randomized controlled trial. *BMC Womens Health*. 2012;12:25.

4. Dysmenorrhea. Medscape Website. http://emedicine.medscape.com/article/253812-overview#a0101 . Accessed October 6, 2014.