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Diclofenac Potassium Attenuates Dysmenorrhea and Restores Exercise Performance in Women With Primary Dysmenorrhea

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Abstract: **We assessed the efficacy of diclofenac potassium, a nonsteroidal anti-inflammatory drug, in alleviating menstrual pain and restoring exercise performance to that measured in the late-follicular phase of the menstrual cycle. Twelve healthy young women with a history of primary dysmenorrhea completed, in a random order, laboratory exercise-testing sessions when they were in the late-follicular (no menstruation, no pain) phase of the menstrual cycle and when they were experiencing dysmenorrhea and receiving, in a double-blinded fashion, either 100 mg of diclofenac potassium or placebo. We assessed the women's leg strength (1-repetition maximum test), aerobic capacity (treadmill walking test), and ability to perform a functional test (task-specific test). Compared with placebo, diclofenac potassium significantly decreased dysmenorrhea on the day of administration (Visual Analog Scale, $P < .001$ at all times). When receiving placebo for menstrual pain, the women's performance in the tests was decreased significantly, compared with when they were receiving diclofenac potassium for menstrual pain ($P < .05$) and compared with when they were in the late-follicular phase of the menstrual cycle ($P < .05$ for treadmill test, $P < .01$ for task-specific test and 1-repetition maximum test). Administration of diclofenac potassium for menstrual pain restored exercise performance to a level not different from that achieved in the late-follicular phase of the cycle.**

Perspective: ***In women with primary dysmenorrhea, menstrual pain, if untreated, decreases laboratory-assessed exercise performance. A recommended daily dose of a readily available nonsteroidal anti-inflammatory drug, diclofenac potassium, is effective in relieving menstrual pain and restoring physical performance to levels achieved when the women were in the late-follicular (no menstruation, no pain) phase of the menstrual cycle.***

Key words: *Menstrual pain, nonsteroidal anti-inflammatory drugs, physical performance.*

Primary dysmenorrhea is the cramping pain that women of child-bearing age experience in the lower abdomen just before menstruation, or during menstruation, in the absence of any pelvic pathology.[9,13,17] Reported prevalence rates for primary dysmenorrhea are as high as 50% to 90%,[25,30] with approximately 15% to 33% of women with dysmenorrhea reporting moderate to severe menstrual pain.[1,12,15,35] The pain is believed to result from excessive prostaglandin release, particularly PGF_2-α.[13,21] As progesterone concentrations fall before menstruation, arachidonic acid is released from the endometrial cell membranes and a cascade of prostaglandin synthesis is initiated in the uterus.[21] In comparison to women with eumenorrhea, women with dysmenorrhea have higher concentrations of PGF_2-α in their menstrual fluid.[2,33] PGF_2-α causes vasoconstriction of uterine blood vessels (uterine ischemia) and increased uterine smooth muscle contraction,[19,20] and it is the contraction of the ischemic uterus that is the likely cause of dysmenorrhea.[13]

The detrimental impact of moderate-to-severe dysmenorrhea on the lives of women is under-appreciated.

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Women experiencing moderate-to-severe dysmenorrhea subjectively report decreased physical activity levels and decreased participation in sporting events.[1,5,37,38] As reported in epidemiological studies, dysmenorrhea is the leading cause, in many countries, of recurrent short-term school and work absenteeism in adolescent girls and women,[5,27] and it has a negative impact on social, academic, and sports activities in female adolescents.[5]

In laboratory-based studies investigating the effect of the menstrual cycle phase (follicular phase versus luteal phase) on exercise performance, some measures of athletic performance were found to be decreased in the luteal (days 15 to 28) phase of the menstrual cycle, compared with the follicular (days 1 to 13) phase of the menstrual cycle.[26,29] Although some of these studies investigated measures of exercise performance in the early follicular phase (eg, day 1 to day 6 of the menstrual cycle) when the women were menstruating, the women were not experiencing moderate-to-severe menstrual pain. As yet, no studies have investigated whether exercise performance in women with moderate-to-severe menstrual pain, compared with the late-follicular phase (no menstruation, no pain), is indeed decreased.

Nonsteroidal anti-inflammatory drugs (NSAIDs), which decrease the formation of PGF_2-α, are effective in alleviating dysmenorrhea.[5,25] Indeed, NSAIDs are the most common pharmacologic treatment for dysmenorrhea.[21] The various formulations of NSAIDs have comparable efficacy for dysmenorrhoea, and pain relief is successfully achieved in between 64% to 100% of women.[31,36] Although the analgesic efficacy of NSAIDs has been well documented, no study has investigated whether attenuation of dysmenorrhea is associated with restoration of exercise performance, if that performance indeed is compromised by dysmenorrhea.

The aim of our study was 2-fold. First, we aimed to assess whether moderate-to-severe dysmenorrhea decreases the exercise performance of healthy women in laboratory exercise performance tests, and, if so, to quantify the decrease in exercise performance. Second, we aimed to determine whether diclofenac potassium, which has been proven to attenuate dysmenorrhea,[8,31] would restore any decreases in the women's exercise performance to levels measured when the women were in the late-follicular (no menstruation, no pain) phase of the menstrual cycle.

Methods

Subjects

Subject Recruitment and Screening Questionnaires

University students were interviewed to assess their eligibility to participate in the study. Using a questionnaire, we obtained information regarding menstrual histories (age of onset of menses, length of cycle, age of onset of primary dysmenorrhea, timing and duration of pain, associated symptoms, severity of the pain, debilitation experienced, and any treatment interventions which successfully alleviated the pain). From the women's menstrual cycle history and onset and duration of menstrual pain, we were able to identify women who fulfilled Dawood's criteria for primary dysmenorrhea[13] and exclude women whose symptoms of pain were more indicative of secondary dysmenorrhea. For their menstrual pain to be classified as primary dysmenorrhea, the women's menstrual pain needed to have begun within 2 years after menarche and occur just before menstruation or during menstruation. Recent onset of pain, or pelvic pain occurring at other times of the menstrual cycle, for example, in the luteal phase, is more indicative of secondary dysmenorrhea and is related to pelvic abnormalities such as endometriosis and uterine malformations.[9,13,20,21] Women with a history of menstrual symptoms more indicative of secondary dysmenorrhea were not included in the study. Only women who rated their menstrual pain above 60 mm (moderate-to-severe) on a 100-mm visual analog scale, (VAS) anchored at "no pain" and "worst pain ever felt," were included in the study.

The women completed a general health questionnaire that screened them for chronic illnesses, joint and muscular abnormalities, and use of chronic medication. Women who were not healthy and who had taken long-term medication or hormonal therapy (oral contraceptives) in the previous 12 months were not included in the study.

Based on the above criteria, 12 healthy null-partum university students, ages 19.6 $\pm$ 1.7 years (mean $\pm$ SD) and with a body mass index of 22.6 $\pm$ 3.4 $kg.m^2$, participated in the study. The women had not taken any long-term medication or hormonal contraception in the 12 months before the study. The women had experienced moderate-to-severe menstrual pain in the past year and did not experience uterine pain from pathology indicating secondary dysmenorrhea. Five of the women routinely attempted to manage their menstrual pain using mild combination analgesics, which they considered to be unsuccessful in treating the pain. Two of the women were self-medicating occasionally with an NSAID and reported adequate pain relief when the NSAID was taken. The remaining 5 women were not taking medication. Except for those who were self-medicating with the NSAID, the women were dissatisfied with their current management strategies for their dysmenorrhea and had accepted their menstrual pain as a normal and intractable female experience.

Level of Physical Activity

The women were required to complete a physical activity questionnaire describing their type and level (frequency, duration, and intensity) of physical activity. The information from the questionnaire was used to design an exercise testing protocol that would be manageable for the women to safely complete. None of the women were participating in structured exercise programs and described walking as their main source of physical exercise.