Combined oral contraceptives in women with menstrual migraine without aura

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Objective: To compare the efficacy of two regimens (21 active pills + 7 placebo pills vs. 24 active pills + 4 placebo pills) of combined oral contraception (COC), both containing 20 μg of ethinyl E_2 and 3 mg of drospirenone, in improving the severity of pure menstrual migraine without aura.
Design: Prospective randomized study.
Setting: Patients attending the gynecology department of the University of Siena for consultation regarding an appropriate contraception.
Patient(s): Women ages 20 to 35 years (n = 60) suffering from pure menstrual migraine without aura.
Intervention(s): Three months of contraceptive use (ethinyl E_2 20 μg/drospirenone 3 mg) in two different regimens: group A received 21 active + 7 placebo pills whereas group B received 24 active + 4 placebo pills.
Main Outcome Measure(s): Monthly evaluation of the duration and severity of patients' daily headache attacks.
Result(s): Although both study groups demonstrated significant reduction in the intensity and duration of menstrual migraine, patients in group B (24/4 COC) reported a significant reduction in the intensity and a shorter duration of their menstrual migraine, compared with group A (21/7 COC).
Conclusion(s): The 24/4 COC regimen is recommended as the preferred treatment for patients suffering from pure menstrual migraine without aura. (Fertil Steril® 2011;96:917–20. ©2011 by American Society for Reproductive Medicine.)

Key Words: Contraception, drospirenone, headache, hormone-free interval, migraine without aura

Migraine, defined as a unilateral, pulsatile headache lasting for 4–72 hours, may be associated with phonophobia or photophobia, nausea and vomiting, and occasionally with simultaneous focal neurologic or visual symptoms referred to as auras. The International Headache Society identifies two different type of migraine linked to menstrual cycle: pure menstrual migraine without aura and menstruation-related migraine without aura (1). Pure menstrual migraine is defined as migraine attacks occurring on or between day 1 of menstruation ± 2 days (i.e., on or between days −2 to +3 of the cycle, assuming day 1 is the first day of menstruation and that there is no day 0), in at least two of three cycles, with no migraine at other times of the cycle. On the other hand, menstruation-related migraine is defined as up to four attacks of migraine per month, of which one must occur on or between day 1 of menstruation ± 2 days, in at least two of three cycles.

Migraine affects women more than men, and approximately 60% of women with migraine reported an association between menstruation and the occurrence of migraine attacks (2). Indeed, the fall in sex steroid levels (e.g., estrogens) may result in an imbalance between the opioid and serotonergic neuron effects, leading to the onset of pain (3). These observations may suggest a possible interaction between migraine attacks and female sex hormones.

In patients using combined oral contraception (COC), migraine headaches appear to be associated with the contraceptive hormone-free interval. The addition of supplemental E_2 during the perimenstrual period (4), and extending or continuing the administration of hormonally active COC pills (5–7), has improved symptomatology and was associated with an overall reduction in migraine severity and frequency (5–7).

The low-dose COCs used nowadays contain the same estrogen component (ethinyl E_2) but vary in their progestin component. Although the majority of progestins used in COCs (norethindrone, levonorgestrel, desogestrel, and norgestimate) are derivatives of 19-nortestosterone, drospirenone, a spironolactone derivative, was shown to significantly improve the physical and behavioral symptoms of premenstrual syndrome and premenstrual dysphoric disorder, attributed to its unique antimineralocorticoid activity (8). Moreover, although studies using validated instruments have shown improvement in premenstrual syndrome with drospirenone-containing COCs, headaches have not been specifically addressed (8, 9). Furthermore, the currently available studies comparing extended COC regimens without a monthly 7-day placebo to the standard 21/7-day regimens are limited and did not evaluate menstrual migraine (5–7) or compare the COC regimen 24/4 with 21/7.

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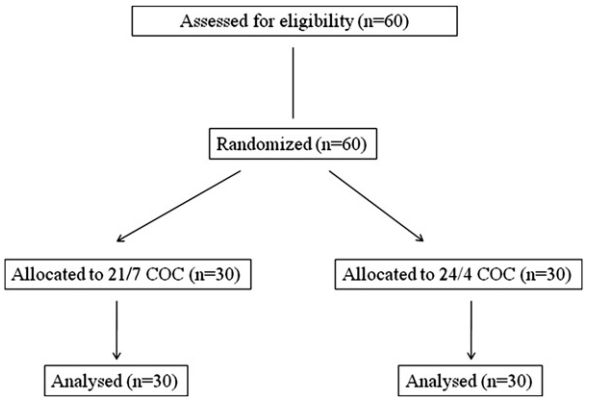
FIGURE 1

Participants flowchart.



De Leo. Oral contraceptives in menstrual migraine without aura. Fertil Steril 2011.

Prompted by the aforementioned observations, we aim to prospectively compare the efficacy of COC containing 20 μg of ethinyl E_2 and 3 mg of drospirenone used in two different regimens: 21 active + 7 placebo pills vs. 24 active + 4 placebo pills on the symptomatology of pure menstrual migraine without aura.

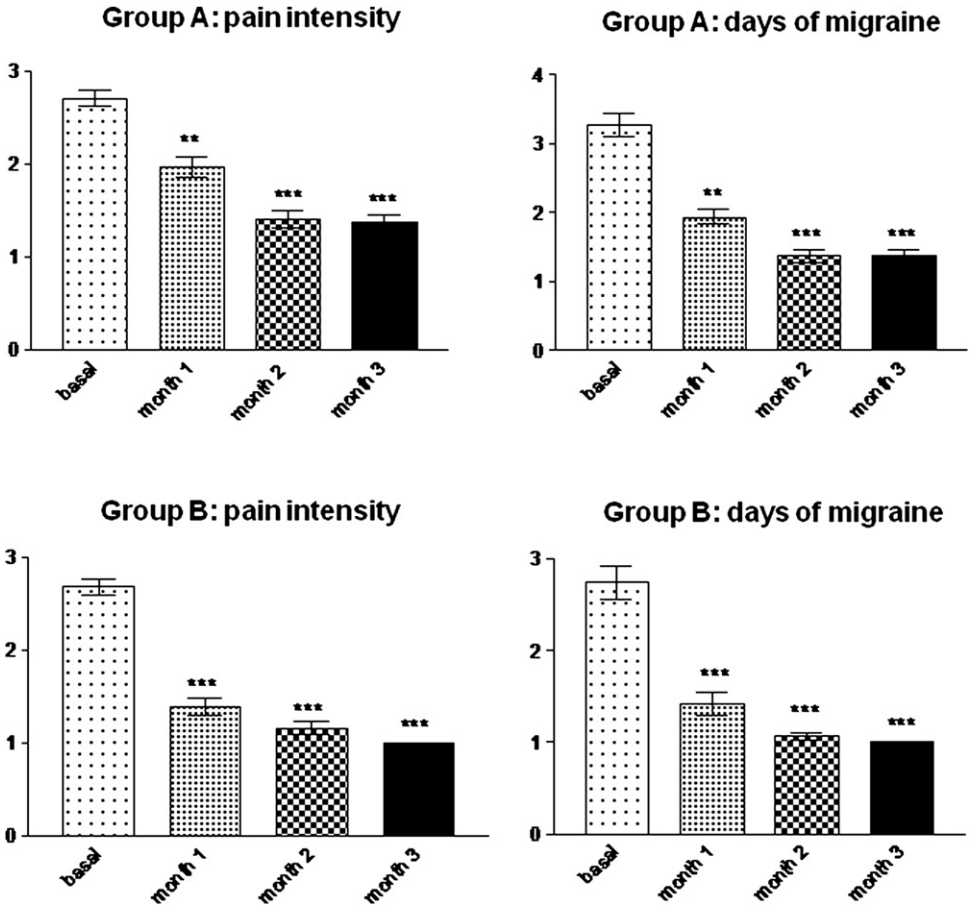
MATERIALS AND METHODS

The study population consisted of all patients attending the gynecology department of the University of Siena for consultation regarding an appropriate contraception. Women who had menstrual migraine according to the criteria of the International Headache Society (an attack of migraine without aura occurring on day 1 of menstruation [day −2 to day +3] in two of three menstrual migraine cycles [1]) were included after a comprehensive neurologic evaluation.

Inclusion criteria also include no COC contraindications, or non-use of hormonal contraceptives for the previous 6 months, aged between 20 and 35 years and in case of patient-smoker, aged 20 to 30 years. Exclusion criteria included pregnancy or lactation, body mass index >30.0, hypersensitivity to any ingredient of the study drug, patients suffering from hypertension, acute and chronic pain other

FIGURE 2

Group A (20 μg of ethinyl E_2 + 3 mg of drospirenone in 21 active + 7 placebo pills) and group B (20 μg of ethinyl E_2 + 3 mg of drospirenone in 24 active + 4 placebo pills), demonstrated a significant reduction in the intensity and a significant shorter duration of menstrual migraine throughout the study period.



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