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INSIDE

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Melatonin and Migraine

By Lynn Keegan, RN, PhD, HNC-BC, FAAN

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Dr. Keegan reports no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study.

MANY THINGS AFFECT QUALITY OF LIFE; AMONG THE MOST DIFFICULT to deal with are migraine headaches. Each year we learn more about the triggers and methods of treatment. We now know that if one parent suffers from migraines, the child has a 50% chance of developing migraine headaches.

Primary headache classifications include migraine, tension, cluster, paroxysmal hemicrania, and miscellaneous headaches unassociated with structural lesions.[1] Chronic migraine is a frequent headache disorder that affects 2-3% of the general population. Analgesic overuse, insomnia, depression, and anxiety are disorders that often are comorbid with this condition.[2] Of the nearly 32 million Americans who suffer with migraine, approximately 24 million are women. Prior to puberty, girls are afflicted with migraine at approximately the same rate as boys, but after puberty there is an emerging female predominance. Although hormones do not entirely explain the epidemiological variation seen in migraine, estrogen plays an important role.[3]

Relationship Between Melatonin and Headache

Discovered approximately 40 years ago, melatonin has been called the "darkness" hormone. Production rises at night, falls by day, and affects the internal body clock and sleep cycles.[4] There is increasing evidence that headache disorders are connected with melatonin secretion and pineal function. Some headaches, such as cluster headaches, have a clear-cut seasonal and circadian pattern. Melatonin levels have been found to be decreased in patients suffering both migraine and cluster headaches.[5] It is interesting to note that the supportive data for use of melatonin seem to be consistent for the past decade.

Melatonin is a human hormone secreted by the pineal gland, a pea-size structure at the center of the brain. Melatonin is produced at night to help the body regulate sleep-wake cycles. The amount produced in the body seems to decrease with aging.

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Treatment with Melatonin

Interest in melatonin is increasing as a result of new discoveries about its role in the biological regulation of circadian rhythm, sleep, mood, aging, tumor growth, and reproduction. Perhaps these processes have led to its use in the treatment of many current problems such as migraine and the control of epileptic seizures.[6] Melatonin may play an important therapeutic role in the treatment of migraines and other types of headaches, particularly those related to delayed sleep phase syndrome.[7] Although a multitude of pharmaceutical agents are available for the treatment of mood disorders, anxiety, and insomnia, many patients have difficulty tolerating the side effects, do not respond adequately, or eventually lose their response. Many therapeutic herbs and nutrients have far fewer side effects and may provide an alternative treatment or can be used to enhance the effect of prescription medications. Melatonin is one of these alternative choices and migraine is one of the disorders.[8] The cornerstone of allopathic maintenance prophylaxis for cluster headache (often masquerading as migraine) is verapamil, yet methysergide, lithium, and divalproex sodium also may be employed. In some patients, melatonin or topiramate may be found useful as adjunctive therapies.[9]

Probable Causes of Migraine

There are a variety of hypothesized causes of migraines, some better documented than others. When seeking an etiology, one might consider the role of the retino-hypothalamic-pineal axis in the pathophysiology of primary headaches in terms of (1) retinal dysfunction, (2) hypothalamic dysfunction and human circadian desynchrony, (3) pineal melatonin dysfunction, and (4) rostral limbic dysfunction mediating the human stress response.[1]

Some think that migraine is caused by a primary biochemical disorder of the central nervous system involving neurotransmitters, specifically serotonin. The pathogenetic mechanism triggered by external and internal stimuli is not well explained or understood. There is a likelihood that the pineal gland, a primary source of central serotonin and melatonin, contributes significantly to migraine attacks.[10]

Another theory suggests that since environmental stimuli are known to trigger migraine headaches, the pineal gland may be involved in migraine etiology. Specifically, a pineal gland irregularity may be the physical origin of migraine headaches, with subsequent physiological changes being secondary. Research has found the pineal hormone melatonin is low in migraine patients.[7]

Nitric oxide supersensitivity is another hypothesis. Its role in causing migraine headaches and chronic morning headaches can be triggered both by normal and abnormal characteristics of the sleep cycle and more specifically by the release of nitric oxide that occurs toward the end of the sleep cycle. Stress and the age-related loss of sleep continuity, together with the corresponding increase in cortisol levels, potentiate delta rebound. Delta rebound results in deeper sleep intensity. It is associated with increased nitric oxide production. Increased delta rebound then causes an increase in the amount and duration of nitric oxide release at night. Migraineurs are susceptible to migraine headaches because they are supersensitive to nitric oxide. The diurnal pattern of the incidence of sleep-related headaches in a subset of the general population is caused by the effect of nitric oxide supersensitivity during the sleep cycle.[11]

Mechanism of Action

Melatonin mechanisms of action are related to headache pathophysiology in many ways, including its anti-inflammatory effect, toxic free radical scavenging, reduction of proinflammatory cytokine up-regulation, nitric oxide synthase activity and dopamine release inhibition, membrane stabilization, GABA and opioid analgesia potentiation, glutamate neurotoxicity protection, neurovascular regulation, serotonin modulation, and the similarity of chemical structure to that of indomethacin.[5,12]

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AHRQ Issues Report on the Safety and Effectiveness of Melatonin Supplements

An evidence review conducted by Health and Human Services' (HHS) Agency for Healthcare Research and Quality (AHRQ) found that melatonin supplements, which people often take for problems sleeping, appear to be safe when used over a period of days or weeks, at relatively high doses and in various formulations. However, the safety of melatonin supplements used over months or even years is unclear. Although there is some evidence for benefits of melatonin supplements, for most sleep disorders the authors found evidence suggesting limited or no benefits. But the authors say that firm conclusions cannot be drawn until more research is conducted. The report was requested and funded by the National Center for Complementary and Alternative Medicine (NCCAM), a part of HHS' National Institutes of Health.

The report's authors reviewed the scientific evidence to date for the benefits of melatonin supplements used for disorders due to sleep schedule alterations and primary and secondary sleep disorders. Disorders due to sleep schedule alterations can stem from flying across time zones or working night shifts. Primary sleep disorders, which include insomnia, can be caused by factors such as stress or drinking too much caffeinated coffee. Secondary sleep disorders also can include insomnia, but patients in this category also have underlying mental disorders, such as psychoses or mood and anxiety disorders, neurological conditions such as dementia and Parkinson's disease, or chronic pulmonary disease.

Clinical Application

In its natural form, melatonin is produced by the brain's pineal gland to regulate the sleep cycle. In the evening the level of the hormone in the bloodstream rises sharply, reducing alertness and inviting sleep, and in the morning it falls back, encouraging waking.

Among those problems for which melatonin supplements appear to provide little benefit are jet lag—a problem that often nags coast-to-coast travelers and those who fly through other time zones, as well as people who work night shifts.

In contrast, the authors found evidence to suggest that melatonin supplements may be effective when used in the short term to treat delayed sleep phase syndrome in persons with primary sleep disorders. In delayed sleep phase syndrome, a person's internal biological clock becomes "out of sync," making it difficult to fall asleep until very late at night and to wake up early the next morning. But melatonin supplements may decrease sleep onset latency—the time it takes to fall asleep after going to bed—in persons with primary sleep disorders such as insomnia, although the magnitude of the effect appears to be limited.

Melatonin supplements do not appear to have an effect on sleep efficiency in persons with primary sleep disorders, and the effects of the hormone do not seem to vary by the individual's age, type of primary sleep disorder, dose, or length of treatment. Sleep efficiency refers to the percent of time a person is asleep after going to bed. Furthermore, melatonin supplements do not appear to affect sleep quality, wakefulness after sleep onset, total sleep time, or percent of time spent in rapid eye movement (REM) sleep. This most important phase of sleep is characterized by extensive physiological changes such as accelerated breathing, increased brain activity, REM, and muscle relaxation.

In people with secondary sleep disorders, melatonin supplements do not appear to have an impact on sleep latency in either adults or children—regardless of dose or duration of treatment. On the other hand, the hormone does appear to increase sleep efficiency modestly, but not enough to be considered clinically significant. Melatonin supplements were not found to have an effect on wakefulness after sleep onset or percent of time spent in REM sleep, but they do appear to increase total sleep time.

"Having evidence on what works and what may have limited or no benefit for the patient is a key part of AHRQ's mission," said AHRQ Director Carolyn M. Clancy, MD. "Sleep disorders can affect a person's quality of life and job performance, which can translate into decreased productivity, motor vehicle and industrial accidents, and even medical errors." Estimates show that at least 40 million Americans each year suffer from chronic sleep disorders, and an additional 20 million experience occasional sleep problems.

NCCAM Director Stephen E. Straus, MD, said, "The data from this report provide not only a scientific perspective on what is known and not known about melatonin to date, but some intriguing and important leads for areas of future research on melatonin and its use for sleep problems. This supplement is of interest to many Americans as an alternative to prescription drugs for this purpose."

The evidence report was prepared by a team of researchers led by Terry Klassen, MD, director of AHRQ's University of Alberta/Capital Evidence-based Practice Centre in Edmonton, and Chair of Pediatrics for the university's Faculty of Medicine and Dentistry. A summary of Melatonin for Treatment of Sleep Disorders can be found at www.ahrq.gov/clinic/epcsums/melatsum.htm. To download the full report as a PDF file, go to www.ahrq.gov/clinic/evrpt-pdfs.htm#melatonin.

Source: AHRQ Issues New Report on the Safety and Effectiveness of Melatonin Supplements. Press Release, Dec. 8, 2004. Agency for Healthcare Research and Quality, Rockville, MD. www.ahrq.gov/news/press/pr2004/melatnpr.htm.

Melatonin is involved in the regulation of seasonal and circadian fluctuations of other hormones and in the synchronization of many different aspects of circadian rhythmicity to the light-dark cycle. In addition to these receptor-mediated functions, melatonin may act as a modulator of intracellular signal transduction to enhance or suppress the responses of many different cells to other incoming signals. This hormone also is a potent scavenger of reactive oxygen species and thus may protect cells and tissues against radical-mediated damage. The production of melatonin declines with increasing age, and circulating melatonin levels are affected by certain pharmacological or physiological manipulations, notably food restriction which increases melatonin levels and prevents its age-related decline.[13]

Clinical Trials

One proposed treatment for both sleep-related migraine headaches and chronic morning headaches consists of melatonin and moclobemide taken at night.[11] Both melatonin and moclobemide affect three important aspects of sleep-related headaches: nitric oxide supersensitivity, stress system dysfunction, and sleep pathology. Both melatonin and moclobemide have demonstrated effectiveness in preventing migraine headaches. Additionally, both melatonin and moclobemide are compatible with most of the other therapeutic agents used to prevent migraine headaches and with at least one therapeutic agent that is used to treat migraine headaches.

A Norwegian university research team investigated potential seasonal variation of migraine and other headaches in an Arctic population where light conditions are extreme during both winter and summer.[14] Because of the immense seasonal variation in sunlight, focus on seasonal migraine variation in a population living in an Arctic area is interesting even from a theoretical point of view. Northern Norway comprises the three Norwegian counties north of the Arctic Circle. There are three neurology centers in this region, which provide service for approximately half a million people. During a two-year period, 1,403 patients (0.3% of the population) were referred to these centers for a specialist assessment of their headaches. A questionnaire was mailed to all of these patients (with a 75% response rate). The questionnaire included questions on headache characteristics to make it possible to identify migraine according to the International Headache Society criteria. Questions on seasonal variation of headache also were included. Nineteen percent reported that their headaches clearly did vary with season; 11% experienced more headache during polar night, while 7% had more symptoms during midnight sun season. When the migraine and nonmigraine groups were compared, significant differences were demonstrated. Patients with nonmigrainous headache were more likely to have increased headaches during the dark winter season, while patients with migraine experienced more headache during the summer ($P = 0.002$). These findings support the increased light sensitivity and recently demonstrated cortical hyperexcitability in patients with migraine, and may perhaps suggest a role of the hypothalamus and/or melatonin secretion in migraine pathophysiology.

Later research conducted in France examined the sensitivity to light of melatonin secretion in familial migraine during a headache-free interval.[15] Twelve female patients and 12 healthy controls were included in the trial. All subjects were studied twice. In each session, light exposure (300 lx) or placebo was randomly administered for 30 min between 00:30 and 01:00 h. Blood was sampled hourly between 20:00 and 24:00 h, and 02:00 and 04:00 h and every 15 min between 00:30 and 01:30 h. Plasma melatonin levels were determined by radioimmunoassay. Melatonin suppression was more marked in the migraine group than in the control group. These findings show a clear hypersensitivity to light in young female migraineurs during the headache-free period.

Hypothalamic dysfunction has been implicated in the pathogenesis of migraine, but it has never been studied in patients with chronic migraines. A Brazilian study analyzed the hypothalamic involvement in this group by measurement of melatonin, prolactin, growth hormone, and cortisol nocturnal secretion.[2] A total of 338 blood samples (13 per patient) from 17 patients with chronic migraines and nine age- and sex-matched healthy volunteers were taken. Melatonin, prolactin, growth hormone, and cortisol concentrations were determined every hour for 12 hours. The presence of comorbid disorders also was evaluated. The results discovered an abnormal pattern of hypothalamic hormonal secretion in those with chronic migraines. This included: (1) a decreased nocturnal prolactin peak, (2) increased cortisol concentrations, (3) a delayed nocturnal melatonin peak in patients with chronic migraine, and (4) lower melatonin concentrations in migraine patients with insomnia. Growth hormone secretion did not differ from controls. These results support hypothalamic involvement in chronic migraine sufferers, shown by a chronobiologic dysregulation, and a possible hyperdopaminergic.

Safety Concerns

In a Canadian study of 13 electronic databases and reference lists of relevant reviews and included studies, results indicated that there is evidence that melatonin is safe with short-term use.[16] (*See article on page 43.*)

Dosage

The recommended dose is 3 mg, taken within 30 minutes before bedtime.[17] Melatonin is sold in 1.5 and 3 mg tablets. The appropriate dose can vary from person to person. It is suggested that one start with a 1.5 mg tablet each night before bedtime, working up to larger doses of 3 mg if needed.[18]

Conclusion

Frequent and recurrent migraine headaches can, over time, pose the additional risks of stroke, brain damage, heart failure, and attention deficit. This is why prevention should always be a part of the treatment.[11] There is evidence that melatonin may play a role in the biological regulation of circadian rhythms, sleep, mood, and aging. Altered melatonin levels in cluster headache and migraine sufferers have been documented.[12]

Current research supports the hypothesis that migraines are a response to a pineal circadian irregularity in which the administration of melatonin normalizes this circadian cycle; i.e., melatonin may play a role in resynchronizing biological rhythms to lifestyle and subsequently relieve migraines and other forms of headaches. In addition, research testing the administration of melatonin found it safe in migraine sufferers, with few or no side effects.[7] For melatonin to become as a more standardized therapy, larger, randomized control trials are needed to confirm that its use to migraine patients is effective. ❖

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Black Cohosh and St. John's Wort Combination for Menopausal Complaints

By Donald Brown, ND

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Dr. Brown is a consultant for Nature's Way, Inc.

Source: Uebelhack R, et al. Black cohosh and St. John's wort for climacteric complaints: A randomized trial. *Obstet Gynecol* 2006; 107:247-255.

Abstract: In a double-blind, randomized, placebo-controlled trial, the efficacy of a combination of a standardized black cohosh extract and standardized St. John's wort extract was studied in women complaining of menopausal symptoms

that included depression. Three hundred and one women (ages 45-60 years) experiencing climacteric complaints (menopausal symptoms) with a "pronounced psychological component" (i.e., depression) were entered in the trial. Inclusion criteria were: (1) climacteric complaints for at least three months; (2) complaints untreated for at least two months; (3) Menopause Rating Scale (MRS) score of 0.4 or more in at least three items; (4) Hamilton Depression Rating Scale (HAM-D) total score of 15-23 points; and (5) HAM-D item 1 score of ≥ 2 points.

Participants were randomized to receive either two tablets bid of a fixed combination of an isopropanolic extract of black cohosh (*Cimicifuga racemosa*; Remifemin®) and an ethanolic extract of St. John's wort (*Hypericum perforatum*; combination produced by Schaper and Brümmer GmbH & Co. KG, Salzgitter, Germany) for the first eight weeks followed by one tablet bid for weeks 8-16 or a matching placebo. Each tablet contained black cohosh extract standardized to 1 mg triterpene glycosides (corresponding on average to 3.75 mg native extract and 22.5-41.25 mg rootstock/rhizome) and St. John's wort extract standardized to 0.25 mg total hypericin (corresponding to 70 mg native extract and 245-350 mg of the herb).

The primary outcome measure was the change in the MRS from baseline to week 16. The MRS is a 10-item scale with each item being scored from 0 (no complaints) to 1 (severe complaints) in increments of 0.1. Symptoms rated include hot flashes, sleep disorders, joint and muscle symptoms, nervousness, disorders of sexuality, depressive moods, impaired memory, vaginal dryness, cardiac complaints, and urinary complaints. For this study, MRS items were grouped into four factors: hot flashes (items 1 and 3), atrophy (items 7-9), psyche (items 4-6), and soma (items 2 and 10). Secondary outcome measures included the HAM-D, the Clinical Global Impressions (CGI), and patient self-assessment. Patients were evaluated at baseline, week 8, and week 16.

A total of 294 women completed the 16-week study. Compared to baseline, the mean MRS total score was decreased in the treatment group by 34.8% at week 8 and 50% at week 16 compared to 21.7% and 19.6%, respectively, in the placebo group. The group difference between baseline and 16 weeks (mean group difference 0.141 ± 0.015; 95% confidence interval 0.112-0.171) as well as between baseline and week 8 was significant ($P < 0.001$). Superiority of treatment compared to placebo was noted for l0 items on the MRS, including hot flashes with a decrease of 53.4% at week 16 in the treatment group compared to 25.4% in the placebo group ($P < 0.001$). The HAM-D total score decreased by 41.8% (18.9 ± 2.2 to 11.0 ± 3.8 points) in the treatment group and 12.7% (18.9 ±2.1 to 16.5 ± 4.3) in the placebo group ($P < 0.001$). According to the CGI, treatment was judged to be "moderate" or "very good" for 78.8% of the treatment group compared to 14.9% for the placebo group ($P < 0.001$). There were no significant differences between groups in adverse events or in treatment tolerability.

■ COMMENTS

DEPRESSION AND ANXIETY ARE NOT UNCOMMON SYMPtoms in women during menopause. In fact, some drug research has focused on use of selective serotonin reuptake inhibitors (SSRIs) in low doses to treat hot flashes.[1] The results to date have been poor. Although black cohosh extract has been shown in numerous studies to adequately address vasomotor symptoms, such as hot flashes, its effect on mild-to-moderate depression is not significant.[2]

Taking a page from traditional herbal medicine and combining two herbs with different mechanisms of action, this interesting clinical trial suggests that the combination of black cohosh and St. John's wort safely and effectively reduced menopausal symptoms such as hot flashes and depression. Practitioners should note the lower dose of St. John's wort used in this trial compared to those that have measured its efficacy alone for mild-to-moderate depression. It is interesting to note that a rather obscure 1999 clinical trial found that 900 mg/d of St. John's wort extract for 12 weeks effectively treated both vasomotor symptoms and depression in menopausal women.[3] This trial used a dose of 900 mg/d and was not placebo-controlled. The combination product used in this trial is available commercially in Europe but not in the United States.

It should be noted that the daily dose of black cohosh and St. John's wort extracts was approximately 80 mg/d and 1,200 mg/d, respectively for the first eight weeks and 40 mg/d and 600 mg/d, respectively for the last eight weeks of the trial. Therefore, the dose of black cohosh for the first half of the trial was roughly double the dose used in more recent trials of black cohosh, and the dose of St. John's wort was 300 mg/d greater than the standard 900 mg/d used in most depression trials with the extract. The dose of black cohosh used in the second half of the trial is more in line with that used in more recent trials.

The results of this clinical trial suggest that the combination of black cohosh and St. John's wort may be useful in treating both vasomotor symptoms associated with menopause as well as depression. Future trials should focus on a more standardized dosage regimen and also include comparisons with black cohosh and St. John's wort alone. Current case reports in the literature and pharmacological studies suggest that St. John's wort should not be used concomitantly with cyclosporine, indinavir, irinotecan, digoxin, warfarin, theophylline,

carbamazepine, phenprocoumon, and amitriptyline hydrochloride. It also should be used cautiously in women taking oral birth control pills. Due to risk of serotonin syndrome, it also is contraindicated in patients taking SSRIs. ❖

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CME Objectives

After reading *Alternative Therapies in Women's Health*, the health care professional will be able to:

1. evaluate alternative medicine and complementary therapies for women's health concerns;
2. identify risks and interactions associated with alternative therapies;
3. discuss alternative medicine options with patients;
4. offer guidance to patients based on latest science and clinical studies regarding alternative and complementary therapies.

CME Instructions

Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity, you must complete the evaluation form provided and return it in the reply envelope provided at the end of the semester to receive a certificate of completion. Upon receipt of your evaluation, a certificate will be mailed.

CME Questions

21. Chronic migraine is a frequent headache disorder that affects:

a. 1-2% of the general population.
b. 2-3% of the general population.
c. 5-6% of the general population.
d. more than 8% of the general population.

22. Melatonin may play an important therapeutic role in the treatment of migraines and other types of headaches, particularly those related to delayed sleep phase syndrome.

a. True
b. False

23. The recommended dosage of melatonin taken within 30 minutes before bedtime is:

a. 1 mg.
b. 2 mg.
c. 3 mg.
d. 4 mg.

24. The results of a recent clinical trial suggest that the combination of black cohosh and St. John's wort may be useful in treating both vasomotor symptoms associated with menopause as well as depression.

a. True
b. False

Answers: 21. b, 22. a, 23. c, 24. a.

News Briefs

Researchers Report Adverse Interaction Between Chamomile and Warfarin

Researchers at the McGill University Health Centre (MUHC) in Montreal have documented a severe case of internal hemorrhaging in a patient who drank chamomile tea and used chamomile lotion while taking anticoagulant medication for a heart condition.

Chamomile tea is taken to treat a range of ailments, including toothache, sore throats, digestive problems, and insomnia. Chamomile lotion often is used to treat the skin conditions psoriasis, eczema, and acne, as well as to help soothe insect bites.

The 70-year-old woman was admitted to the MUHC emergency room after using chamomile to help soothe her sore throat. She had been implanted with a mechanical valve and was taking the anticoagulant medication

warfarin. Several factors led caregivers to the possibility of a chamomile/warfarin interaction. First, the patient's daughter verified her medications and said there was no possibility of warfarin overdose during the time in question. Second, a consultation with the patient's pharmacist revealed no change in warfarin dosage over the previous 11 months. Review of the patient's other medications also did not reveal any potential interactants with warfarin, and the patient consumed no antiplatelet agents at any time. In addition, the patient said she had not changed her diet in the days before her hospital admission.

The patient, however, revealed that she had been using a chamomile-based skin lotion to help treat her pedal edema. For this, she applied a teaspoon-sized amount to each leg four to five times per day. She also used a camphor-based lotion to ease her chest congestion and drank four to five cups a day of chamomile tea, prepared by adding water to a teaspoon of dried chamomile leaves, to try to ease her sore throat. She usually used both chamomile products once or twice per day, the researchers say.

As a result of the previous questioning and the chamomile use, caregivers linked the occurrence of this hemorrhage to the simultaneous and excessive use of chamomile products.

"We are aware of several herbal products that should not be taken with warfarin, such as garlic, onion, and ginger, but this is the first time we have documented a life-threatening reaction when combined with chamomile," says Louise Pilote, MD, MPH, PhD, an internist and epidemiologist at the MUHC and associate professor of medicine at McGill University. She is also one of the authors of the research, published in the April 25 issue of the *Canadian Medical Association Journal*.

Warfarin is derived from coumarin, a chemical compound with anticoagulant properties found in many plants, including chamomile. "It seems the chamomile acted synergistically with the warfarin in this case," Pilote says. "Although this is a rare case, it highlights the potential dangers of mixing herbal remedies with physician-prescribed medications."

Because of the possible interaction, the researchers say, patients should be educated about the potential risk of using chamomile products while being treated with warfarin.

Women who Reduce Milk Intake During Pregnancy May Have Smaller Babies

New research shows that women who consumed one cup or less of milk per day gave birth to infants who weighed less than those born to women who consumed more milk, although infant lengths and head circumferences remained similar. Women who restricted milk intake also had statistically significantly lower intakes of protein and vitamin D.

The researchers say that some pregnant women are being advised or are choosing to restrict milk consumption and may not be taking appropriate supplements. The researchers hypothesized that maternal milk restriction during pregnancy, which can reduce intakes of protein, calcium, riboflavin, and vitamin D, might represent a health risk by lowering infant birth weight.

They studied 72 women between the ages of 19 and 45 years who admitted to restricting milk and were attending prenatal programs in Calgary, Alberta, Canada. Using dietary recalls compiled from telephone interviews, the researchers compared these women and their babies with babies to women whose daily milk consumption exceeded 250 mL (1 cup). Birth weight, length, and head circumference were obtained from birth records.

In multivariate analyses controlled for previously established predictors of infant birth weight, the researchers found milk consumption and vitamin D intake both to be significant predictors of birth weight. Each additional cup of milk daily was associated with a 41 g increase in birth weight, and each additional mcg of vitamin D was associated with an 11 g increase. Neither protein, riboflavin, nor calcium intake was found to predict birth weight. The findings of the research were published in the April 25 issue of the *Canadian Medical Association Journal*.

Absence of vitamin D seems to be driving the results, study co-author Kristine G. Koski, PhD, tells Reuters Health. Koski is director of the School of Dietetics and Human Nutrition at McGill University in Montreal, Canada. The vitamin D intake for the women who restricted milk was still, on average, within the recommended range. This suggests that pregnant women need more than the current "adequate" intake level for vitamin D—5 mcg for adults age 50 and younger, Koski tells Reuters. ❖

In Future Issues:

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