Int J Fertil, 51(3), 2006 p. 125–129

Menopace® Nutrient Therapy: An Alternative Approach to Pharmaceutical Treatments for Menopause

Russell S. Kirby, PhD, MS, FACE

Department of Maternal and Child Health
School of Public Health
University of Alabama at Birmingham
Birmingham, Alabama

ABSTRACT: Considerable controversy surrounds the use of hormone replacement therapy (HRT) for treatment of peri-menopausal symptoms. Recent publications from three large, prospective randomized studies call the safety of HRT into question, and leave patients searching for answers. Nutrient therapy may provide symptomatic relief without increasing risk of chronic disease. In this study, results of a series of uncontrolled prospective studies of peri-menopausal symptom relief using Menopace® nutrient therapy were combined to provide a broad perspective on the safety and effectiveness of this alternative treatment modality. Data from seven studies with a total of 766 subjects were analyzed. Subjects with specific menopausal symptoms reported improvement after three months of daily use of the therapy, ranging from 87.8% of subjects with hot flashes to 67.5% of subjects with poor concentration reporting improvement. Overall improvement in menopausal symptoms was reported in 93.2% of all subjects. These results provide consistent evidence of the effectiveness of comprehensive, nutritionally balanced nutrient therapy for treatment of menopausal symptoms. While most evidence-based practitioners focus primarily on research results from randomized, controlled clinical trials, other forms of research evidence can also guide clinicians searching for safe and effective treatment options for their patients. *Int J Fertil* 51(3):125–129, 2006

KEY WORDS: menopause, nutrient therapy, evidence-based practice, uncontrolled prospective studies

AS LIFE EXPECTANCY INCREASES and the population grows throughout the world, more women not only are reaching the age of menopause and living well beyond it, but are also demanding a higher quality of life during these later life stages. Whereas menopause is not a disease *per se* in any sense of the word, it does represent a natural biological process in the human female [1], which is often associated with a range of unpleasant physiological occurrences. In the past, most women put up with the vicissitudes of menopausal changes, believing that there was little that they could do to alleviate them. With the advent of prototype hormonal replacement therapy in the 1960s, however, many women were initially offered estrogen, and later, combinations of estrogen and progesterone, to alleviate the numerous annoying symptoms of this stage of life. Alone or combined, these two hormonal agents became known to medical professionals and the lay public as hormone replacement therapy (HRT).

Recently, HRT has been called into question, most notably through the initial publication and subsequent interpretations of the American Women's Health Initiative study (WHI), the Heart and Estrogen/Progestin Replacement Study (HERS/HERS II), and the British Million Women Study [2,3,4]. The immediateness of the response of clinicians and gynecological professional societies to published results from these studies was not unexpected. This, coupled with a worldwide medical coverage that was little less than sensationalistic, resulted in a dramatic decline in the use of hormonal therapies for women during and after menopause. With time for reflection, the appropriateness of this 'rejection response' has been called into serious question, not only in the United States, but in the United Kingdom as well [5,6,7]. As this debate continues and secondary analyses and counter analyses of these studies continue to appear, many women are bewildered by this conflict and appropriately ask their health care

providers what non-hormonal alternatives might be available to provide relief from the symptoms of menopause. This basic question has resulted in an enormous outpouring of interest in the literature, much of which is related to the discipline of alternative medicine, an area of medicine now so vast that it cannot be addressed in this review.

Having said this, among the currently available alternatives to HRT, there is growing international interest in the potential of using nutrient therapy for treatment of the menopause and its symptomatology [8,9]. Indeed, a large number of manufacturers have developed and marketed nutritional or herbal products for relief and control of menopausal symptoms, but few studies exist that describe the safety and efficacy of these products [10]. This report describes the tolerability, safety, and efficacy of *Menopace®*, a vitamin and nutrient supplement marketed for peri- and postmenopausal women.

METHODS

Menopace® (Vitabiotics Ltd., London UK.) contains a balanced palatte of 22 nutrients selected based on their published properties to maintain women's health during menopause. These nutrients include vitamin B complex, zinc, magnesium, vitamins A, C, D, and E, manganese, chromium, and selenium. For this analysis, study designs and results for all available observational studies of *Menopace®*, in uncontrolled as well as randomized studies, were analyzed to determine which might be included in summary analyses. Specifically, the dosage and recommended frequency of use, the length of follow-up, and the pre- and post-usage symptomatology questionnaires were reviewed for similarities in study design across the studies. All of these studies are unpublished, and reports provided by their authors to Vitbiotics Ltd. were made available for the purpose of this analysis.

Several placebo-controlled trials were reviewed, including two in India and one in Russia. In none of these studies do the research reports document that study subjects were randomized to treatment groups. Moreover, differences in comparison groups, length of follow-up, and other study design issues made it imprudent to include these trials in the summary analyses.

A total of six out of 7 seven uncontrolled observational studies with a combined 766 subjects were amenable to summary analysis. These studies were:

Study	*Place*	*Year*	*Sample*
University of Kent	UK	1992	200
Mirror	UK	1994	200
Soonawala	India	1995	25
Krishna	India	1995	26
Narenda	India	1995	15
Prima	UK	1995	200
Virkud	India	n.d.	100
Total			766

All studies examined the efficacy of *Menopace®* in peri- and post-menopausal women, selected as random samples from contacts made by respondents to an appeal for clinical trial volunteers by the health editors of leading magazines or newspapers, with the exception of the Krishna and Virkud studies, which used the same methods but obtained subjects from large outpatient gynecology practices. Following recruitment, university survey research centers or well-known obstetrician/gynecologists conducted or monitored the investigations. Participants were asked to complete an initial questionnaire and were then provided with a one month supply of *Menopace®*. At the month's end, respondents returned the questionnaire, and received the next month's supply by mail. Of the seven studies, one followed participants for two months and the other six completed three months of follow-up.

RESULTS

Seven observational studies were conducted from 1992 through 1995, in the United Kingdom and India. Although the study patients ranged in age from 24 to 67, the majority of participants were in their 40s or older. Mean ages were reported for six of the seven studies, and ranged from 44 to 53. Some attrition occurred in all the studies. A careful statistical analysis of the characteristics of dropouts and those who continued could not be performed with the available data, though some of the studies themselves attempted to do this. Women who did not continue for the full three months appeared to have had less favorable response from *Menopace®* in terms of their menopausal symptoms.

For the women completing the three month follow-up, symptomatic improvement is shown in Table I, and overall symptom improvement results are presented in Table II. These data suggest that the vast majority of women participating in these observational studies experienced substantial improvement in their menopausal symptoms using

TABLE I
Improvement in menopausal symptoms with three months daily use of *Menopace*®, seven observational studies.

Symptom	*No. with Symptom Prior to Treatment*	*No. with Improvement After 3 months*	*Percent Improvement*	*Range (Percent)*
Hot Flashes	262	230	87.8	48–100
Dry Sweats	214	172	80.4	43–100
Vaginal Dryness	150	117	78.0	22–100
Night Sweats	247	190	76.9	54–100
Depression	176	134	76.1	43–92
Lack of Energy	261	195	74.7	49–100
Palpitations	143	105	73.4	34–100
Anxiety	207	148	71.5	42–95
Poor Concentration	197	133	67.5	47–100

Includes data from University of Kent, Daily Mirror, Prima, Krishna (2 month outcomes only), Soonwala, Virkud, and Narendra studies.

Menopace® daily for three months. Improvement in specific symptoms varied, however. The Daily Mirror study sample contributed the poorest outcomes of any of the studies for each of the specific symptoms reported in Table I. Overall improvement was better in the three observational studies from the United Kingdom than in the four Indian observational studies. Very few side effects were reported in any of the studies, and none of these was significant.

Additional observational studies of the efficacy of *Menopace*® were also conducted. An uncontrolled clinical trial conducted by Prof. V. I. Krasnopolsky at the Moscow Regional Obstetrics and Gynecology Research and Development Institute (Russia) compared menopausal symptoms in peri-menopausal women treated with *Menopace*® (N = 30) and HRT (N=28) with six months of follow-up. Because these results were reported using different clinical outcomes, this study was not included in the summary analysis. However, by six months, the proportion with severe climacteric manifestations in the *Menopace*® arm of the study had declined from 50% at baseline to 10%, similar to that observed among those women receiving HRT. In another study, 120 women with mean age of 50.7 years were followed for three months in gynecology clinics in five Lithuanian cities in 1999 (V. Riauba, Entapharma). Although the results were presented in a manner difficult to include in the summary analysis, almost all patients had at least some overall symptom improvement with three months of daily *Menopace*®, and results for individual symptoms

TABLE II
Overall improvement after 3 months daily use of *Menopace*®, seven observational studies.

Study	*N*	*Some or Significant Improvement*	*Percent with Improvement*
Daily Mirror	90	89	98.9
Kent	75	74	98.7
Soonwala	22	21	95.5
Prima (2 months)	61	58	95.1
Krishna	26	23	88.5
Virkud	90	77	85.6
Narendra	15	11	73.3
Total	379	353	93.2

were in the mid-range of those from the combined analysis. A third study from India compared 60 peri-menopausal women, 30 of whom received placebo and 30 *Menopace®*, and found greater improvements in menopausal symptomatology among women in the *Menopace®* group; unfortunately, this publication did not provide sufficient study design information to determine if the study was a scientifically randomized, controlled clinical trial. Other trials were conducted in Russia, Denmark, and India (Dr. R. Arora, Maulana Azad Medical College, New Delhi) during the early 1990s; however, here also the study designs and methods of analysis were not similar to the majority of trials cited in this report. Despite this, these results were similar to those reported above.

DISCUSSION

The summary analyses presented in Tables I and II suggest that nutrient therapy can play an important role in the treatment of menopausal symptoms. All of the studies formally examined were observational in nature, without control groups and most relied on informant surveys without direct observation or clinical examinations. Despite these limitations, the relatively consistent results across the studies and in different cultures as well as the summary analyses strongly suggest that *Menopace®* may have an important and reliable therapeutic effect in treatment of the menopause.

The studies examined have specific limitations in terms of methodology. Most were uncontrolled, although this is partially offset by the random selection of participants, the consistency of the results obtained, and the fact that the levels of improvement are considerably higher than would be expected for a placebo effect on symptoms such as hot flushes. In the case of the two clinic-based studies, selection bias may have played a role in the identification of the study samples. Because there were no comparison groups, it is impossible to determine whether the observed results differ from those that might have occurred among a placebo group, or compare favorably with other available therapies. However, the levels of symptomatic improvement appear to be greater than those attributable to the placebo effect in similar trials [11]. In addition, as the menopausal symptomatology was not reported using a validated menopause symptomatology instrument [12], the results from these studies cannot be directly compared with other published reports. Further, although difficult to analyze, there appears to be a tendency for those without symptom relief to drop out of the studies. While this was not the case in one of the larger studies (Kent, 1992), it could potentially influence these results. Finally, each of these studies was relatively small, and followed participants only for three months, rather than 12 months or several years.

Having acknowledged these limitations, viewing study results collectively (Table I), evidence exists to support the statement that *Menopace®*, taken daily for as short a period as three months, provides substantial improvement in specific menopausal symptoms for most women.

Future research might address the following questions: How would *Menopace®* fare in a truly controlled trial? How does it compare with other commercially available herbal and vitamin preparations? Is it more or less effective than HRT for treatment of peri-menopausal women, or more effective in combination with HRT? These questions may never be answered due to the complex interplay of the various conditions that surround the undertaking of a randomized, placebo controlled trial.

In recent years, the value of the knowledge gained from observational studies, has come under question as the evidence-based practice paradigm came into increasing use both in medical training and in clinical practice [13]. Observational studies were once the mainstay of medical and scientific investigation, but today, clinicians who are trained in evidence-based programs and schools often believe that clinical decisions can only be made on the basis of research evidence at the highest levels within a hierarchy of study designs and results [14]. Indeed, some practitioners make their decisions only with evidence from randomized controlled clinical trials (RCCT). Although such studies, when properly conducted, provide the highest level of evidence, many situations exist in which RCCTs cannot be conducted. Moreover, older and more experienced clinicians cannot help but remember the numerous examples of now-accepted observations of cause and effect made on the sole basis of observational studies. The classic example of this reality is the British physician's study undertaken by Doll and Hill [15], which provided highly convincing evidence from an observational study for the association between tobacco smoking and lung cancer. Despite the fact that no RCCT was subsequently undertaken, virtually all medical practitioners and public health officials today accept that an etiological link exists between tobacco use and lung cancer as well as other chronic diseases. Other examples also exist,

dating at least to the time of Semmelweiss, who used observational methods to demonstrate the association between unclean hands and puerperal sepsis in an era prior to routine use of gloves for autopsy or obstetrics delivery [16].

Even accepting the fact that RCCTs and meta-analyses based on these studies provide the highest level of evidence, one must still acknowledge that neither type of study exists that relates to numerous questions of clinical concern. Thus, in many situations where RCCTs are not available, clinicians are forced to offer their patients the best possible options for treatment from those that are available. Given this latter set of circumstances, clinicians may still wish to strongly consider the results of observational studies rather than falling victim to the 'tyranny of evidence' and, in the absence of published results from randomized, controlled studies, say that nothing can be done.

Whereas the individual results of the small studies examined here yield incomplete evidence, examined systematically they provide a relatively consistent picture. Ideally, follow-up for at least 12 months would be appropriate to confirm the symptomatic improvements. In offering a nutritional supplement such as *Menopace*® there may also be the spin off benefit of improving the nutritional status and health of the patient. As side effects are minimal, the regime also has the advantage that it may be offered as a long term solution. Clinicians who choose to offer *Menopace*® to their peri- and post-menopausal patients should carefully examine each patient and document their symptoms and complaints prior to treatment, monitor patients periodically to identify its effectiveness for peri- and post-menopausal symptoms, and identify any side effects. Hopefully, these results will be followed by a truly randomized trial of what appears to be a most useful therapeutic option to HRT.

REFERENCES

1. Speroff L, Fritz MA: *Clinical and Gynecologic Endocrinology and Infertility*, 7th Ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2004.
2. Rossouw JE, Anderson GL, Prentice RL, et al: Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA* 288:321–333, 2002.
3. Grady D, Herrington D, Bittner V, et al, HERS Research Group. Cardiovascular disease outcomes during 6.8 years of hormone therapy: Heart and Estrogen/progestin Replacement Study follow-up (HERS II). *JAMA* 288:49–57, 2002.
4. Million Women Study Collaborators: Breast cancer and hormone-replacement therapy in the Million Women Study. *Lancet* 362:419–427, 2003.
5. Naftolin F, Taylor HS, Karas R, et al: The Women's Health Initiative could not have detected cardioprotective effects of starting hormone therapy during the menopausal transition. *Fertil Steril* 81(6):1498–1501, 2004.
6. Machens K, Schmidt-Gollwitzer K: Issues to debate on the Women's Health Initiative (WHI) study. Hormone replacement therapy: an epidemiological dilemma? *Hum Reprod* 18(10):1992–1999, 2003.
7. Speroff L: A clinician's review of the WHI-related literature *Int J Fertil Women's Med* 49:252–267, 2004.
8. Warren MP, Shortle B, Dominguez JE: Use of alternative therapies in menopause. *Best Pract Res Clin Obstet Gynecol* 16:411–448, 2002.
9. Wylie-Rossett J: Menopause, micronutrients, and hormone therapy. *Am J Clin Nutr* 81:1223S–1231S, 2005.
10. Huntley AL, Ernst E: A systematic review of herbal medicinal products for the treatment of menopausal symptoms. *Menopause* 10:465–476, 2003.
11. Irving K, Sapirstein G: Listening to Prozac but hearing placebo: A meta-analysis of antidepressant medication. *Prevention & Treatment* 1, 1, 1998. (www.journals.apa.org/prevention/volume1/toc-jun26-98.html)
12. Schneider HPG: The quality of life in the postmenopausal woman. *Best Practice & Research Clinical Obstetrics and Gynecology* 16:395–409, 2002.
13. Sackett DL, Straus SE, Richardson WS, et al: *Evidence-Based Medicine: How to Practice and Teach EBM*, Second Edition. Edinburgh: Churchill Livingstone, 2000.
14. Report of the U.S. Preventive Services Task Force. Guide to Clinical Preventive Services, Second Edition. Alexandria, VA: International Medical Publishing, 1996.
15. Doll R, Hill AB.: Smoking and carcinoma of the lung: Preliminary report. *Br Med J* 2:739–748, 1950.
16. Carter KC: SemmelWeis and his predecessors. *Med Hist* 25(1): 57–72, 1981.

Address reprint requests to:
Russell S. Kirby, PhD, MS, FACE, Professor
Department of Maternal and Child Health
School of Public Health
University of Alabama at Birmingham
320 Ryals Building, 1530 3rd Avenue South
Birmingham, Alabama 35294-0022
rkirby@uab.edu