

# Evaluation Of The Efficacy And Tolerability Of Micronutrient Supplementation In Treatment Of Post Menopausal Symptoms

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## Abstract

**Objective-** To study the efficacy and tolerability of micronutrient supplementation in alleviating menopausal symptoms. **Method-** In this randomized pilot study, 54 postmenopausal women from the outpatient department were supplemented with either micronutrients or placebo for three months. Along with the menopausal symptoms, hemoglobin and lipid profile were assessed. **Results-** Micronutrients demonstrated moderate to almost complete improvement in symptoms on the 60<sup>th</sup> and 90<sup>th</sup> day of the treatment which was better compared to placebo group. The treatment group reported better improvement in night sweats, insomnia and feeling of well-being on the 60<sup>th</sup> day and almost complete improvement in hot flushes, insomnia, tiredness and feeling of well-being which was significantly better compared to the placebo group ( $p < 0.05$ ) on the 90<sup>th</sup> day of treatment. No side effects were reported in the micronutrient supplement group. **Conclusion-** Our findings suggest that the multiple micronutrient supplements are effective in improving postmenopausal symptoms of hot flushes, night sweats, insomnia, depression, tiredness and for improving feeling of well-being.

## INTRODUCTION

Menopause, commonly known as the “change of life” for women, is a gradual physiological cessation of menses as a result of decreasing ovarian function.

About 75% of women report troublesome symptoms during menopause, but the severity and frequency of symptoms is very inconsistent. The most common symptoms are hot flushes and vaginal atrophy. Other symptoms at the onset include fatigue, irritability, insomnia, depression, night sweats, palpitation and anxiety. The duration of these symptoms is usually one year but last for more than five years in about 25-50% of women.<sup>1</sup> Several hormonal products are available and growing. At the same time, use of dietary products to treat menopausal symptoms is also rising.

Earlier studies state that women with menopause suffer from osteoporosis due to estrogen deficiency. The bone fragility increases with the additional deficiency of Magnesium.<sup>2</sup> Cummings SR concluded that Vitamin D substantially reduced the risk of hip fracture in post menopausal elderly women.<sup>3</sup>

The balanced and appropriate multivitamin and mineral supplements containing vitamins (Vitamin A, Riboflavin, Pantothenic acid, Pyridoxine, Folic acid, Vitamin E) and minerals (chromium, copper, magnesium, selenium, silicon, zinc) are essential for the prevention or correction of disorders accompanying menopause like ageing of skin and its accessory structures, decreased bone metabolism, decreased immune function and increased risk of degenerative pathology, in particular cardiovascular system.<sup>4</sup> Antioxidants like Vitamin C acutely improve the endothelial function in postmenopausal women with established estrogen deficiency.<sup>6</sup> Evidence indicates that postmenopausal women have increased plasma homocysteine level. Folic acid, Vitamin B<sub>6</sub> and Vitamin B<sub>12</sub> is associated with a significant reduction in plasma concentrations of homocysteine. The highest initial levels of homocysteine reduced with the low folic acid doses when given as supplementation in postmenopausal women.<sup>7,8,9,10</sup> All these multiple micronutrient supplements when given in combination, can effectively alleviate the menopausal symptoms. Menopausal women often suffer from common symptoms. Though there is growing need and

interest of using nutrient and other non-hormonal therapies due to the risks of HRT, clinical evidence for efficacy of nutrients in menopausal symptoms is limited. Pertaining to this background, this pilot study was conducted in Indian women.

## **MATERIALS AND METHODS**

This randomized trial was performed to determine and compare the effect of micronutrient supplementation with that of placebo in reducing the menopausal symptoms. Secondary objectives were to compare the effects of both the treatment therapy on lipid profile and hemoglobin. Total fifty four women with in the age group of 40-60 years [(mean age  $\pm$  SD) (48.86 $\pm$ 7.10)] with characteristic menopausal symptoms for at least one year were enrolled in the study. The study was approved by Lokmanya Tilak Hospital Ethics Committee at Sion, Mumbai and was conducted in accordance to applicable regulatory guidelines for clinical trials, Declaration of Helsinki, as revised in 2000. Written informed consent was obtained from all the participants before starting any of the study related procedures. Women with both natural and surgical menopause were included. Women who were on any hormone replacement therapy (HRT); with known history of any hypersensitivity to study drugs; who experienced serious adverse events or hypersensitivity reaction during ongoing treatment were excluded from the study. Subjects were randomized and divided into two groups where group A (N=29) received micronutrient supplementation while group B (N=25) received placebo treatment. The micronutrient supplement (Refer Table-1) was a non-hormonal preparation providing a specific range of vitamins & minerals and assumed to be effective in relieving a large number of symptoms. Micronutrient supplementation was provided by Meyer Organics Pvt Ltd Thane.

Primary efficacy endpoints were improvement in the symptoms including; hot flushes, night sweats, depression, tiredness, insomnia and feeling of well being. The secondary endpoints were improvement in baseline levels of total cholesterol (TC), serum triglycerides (TG) and hemoglobin (Hb). Physical parameters like blood pressure, pulse rate and body weight were evaluated at each visits. Subjects received one oral capsule daily after meal for three months. The improvements in symptoms were graded as mild or minimal (1-25%), moderate to good (26-50%) and almost complete (51-75%) on the 30<sup>th</sup>, 60<sup>th</sup> and 90<sup>th</sup> day of study. The biochemical parameters were also evaluated on the

respective visits. The study subjects were evaluated for occurrence of any adverse events including their intensity, action taken, outcome and causality. Micronutrient supplementation (Menopace<sup>®</sup> Tablets) was provided by Meyer Organics Pvt Ltd Thane

## **RESULTS**

Results were analyzed statistically by the Chi-Square test. P value less than 0.05 was considered significant. The results are presented here.

**Hot Flushes:** At baseline, 20 women each from active and placebo reported presence of hot flushes. On the 90<sup>th</sup> day, 13 women (65%) in micronutrient treatment group as compared to 3 (15%) in placebo group reported almost complete improvement. (P=0.001) Also, 7 (35%) women in treatment group reported moderate to good improvement compared to 11 (55%) in placebo group. 6 (30%) women in placebo group reported minimal or no improvement in hot flushes at the end of treatment period.

**Night sweats:** At baseline, 14 and 12 women reported presence of night sweats in active and placebo group respectively.

On 60<sup>th</sup> day 12 (85.7%) women in micronutrient treatment group experienced moderate to good improvement in night sweats as compared to 6 (50%) in placebo group (P=0.04). Further, on the 90<sup>th</sup> day, 13 (93%) patients in active and 8 (67%) patients in placebo group reported moderate to almost complete improvement in their night sweats.

**Depression:** On the 90<sup>th</sup> day of treatment, 10 (66.7%) women in active group compared to only 2 (22.2%) women in placebo group reported moderate to good improvement in depression. (P=0.03) Overall, 14 (80%) women experienced good to almost complete improvement in depression compared to 4 (45%) in placebo group.

**Tiredness:** At baseline, 18 women in active group and 19 women in placebo group reported presence of tiredness. Improvements were comparable on the 60<sup>th</sup> day. However on the 90<sup>th</sup> day of treatment, 7 (39%) women in micronutrient treatment group experienced almost complete improvement compared to only 1 woman in placebo group (P=0.03).

**Insomnia:** At baseline 15/29 and 16/25 women reported insomnia.

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On the 60<sup>th</sup> day, 14 (93.3%) women reported moderate improvement compared to 10 (62%) in the placebo group (P=0.004) and at the 90<sup>th</sup>, 8 (53%) women reported almost complete improvement as compared to 1 (6.2%) in placebo group. (P=0.004) Also, 8 (50%) women experienced minimal or no improvement in insomnia till the end of therapy period.

Feeling of well-being: At baseline 16 and 14 women had reported feeling of not being well.

Of them 15 (93.8%) women in active group reported moderate to good improvement compared to 8 (57%) in placebo group on the 60<sup>th</sup> day. (P=0.01) Further, on the 90<sup>th</sup> day, all 16 (100%) reported good to almost complete improvement in feeling of well being compared to 8 (57%) in the placebo group. (P=0.02)

Anxiety: At baseline, 18 and 13 women in the active and placebo group reported anxiety, respectively. Out of them, 15 in active group and 8 in the placebo group reported moderate to good improvement at the 60<sup>th</sup> day. Furthermore, at the 90<sup>th</sup> day, all 18 (100%) women in active group compared to 10 (76%) in placebo group reported moderate to good improvement.

Safety assessment: Baseline hemoglobin, total cholesterol & serum triglyceride values did not change significantly at the end of the study. (Table 2) In addition no change was observed in physical examinations including blood pressure, pulse rate and body weight in both the study groups. (Tablet 3) Micronutrient supplementation was found safe and well tolerated.

**Figure 1**

Table 1: Micronutrient composition of tablet (Menopace®)

Micronutrients	Per Tablet
Vitamin A	2500 IU
Vitamin D	100 IU
Vitamin E	30mg
Vitamin B1	10mg
Vitamin B2	5mg
Vitamin B6	40mg
Vitamin B12	9mcg
Vitamin C	45mg
Niacinamide	20mg
Biotin	30 mcg
Folic acid	400mcg
Boron	2mg
Selenium	100mcg
Chromium	50mcg
Iodine	225 mcg
Copper	1mg
Manganese	2mg
Iron	12mg
Magnesium	15mg
Calcium Pantothenate	30mg
Para amino benzoic acid	30mg

**Figure 2**

Table 2: Change in baseline Hemoglobin, Total Cholesterol & Triglyceride

Examinations	Study Group (N = 29)		Control Group (N = 25)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Hb	11.55 ± 1.69	11.54 ± 1.63	11.11 ± 1.44	11.28 ± 1.10
Total Cholesterol	214.48 ± 36.63	206.28 ± 34.51	197.76 ± 37.62	199.79 ± 29.61
Serum TGL	124.47 ± 51.82	159.83 ± 94.19	126.45 ± 39.15	137.76 ± 43.84

By Student's t Test

P > 0.05 Not Significant

**Figure 3**

Table 3: Change in baseline blood pressure (BP) measurement, pulse rate & weight

Examinations	Study Group (N = 29)		Control Group (N = 25)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Systolic BP	118.07 ± 9.68	119.89 ± 7.64	120.80 ± 12.56	119.04 ± 13.83
Diastolic BP	78.00 ± 6.39	79.41 ± 5.57	78.56 ± 9.93	79.84 ± 6.97
Pulse Rate	83.97 ± 4.68	85.56 ± 4.31	87.76 ± 5.30	86.42 ± 6.65
Weight	56.97 ± 10.81	58.64 ± 10.74	52.88 ± 14.48	53.96 ± 12.94

By Student's 't' Test

P > 0.05 Not Significant

## DISCUSSION

To our knowledge this is the first double-blind clinical study conducted to evaluate efficacy of micronutrient supplementation for relieving menopausal symptoms in Indian women. In this study key symptoms of menopause were quantified to assess the effectiveness of micronutrient supplementations in menopause. At the end of the treatment, subjects reported almost complete improvement in hot flushes, insomnia, tiredness, and feeling of well-being. Micronutrient supplements significantly reduced the postmenopausal symptoms and improved general well being suggesting their important role in the treatment of menopausal symptoms. Tolerability and the compliance to the study drug were found to be very good. Our study may be lacking in strong study design with respect to duration of the study and relatively less sample size, but this data may prove useful for the researchers and general population when it comes to multiple micronutrients as a safe and effective option for women.

## CONCLUSION

A non-hormonal nutritional supplement which provides specific range of vitamins and minerals corrects nutritional imbalance and thereby provides relief and prevention from menopausal symptoms. Results obtained from this study supports to the evidence that long-term treatment with micronutrient supplementation could be more effective in improving symptoms related to menopause without any

detrimental effects on women's health. The regimen also appears to be a safe and effective alternative to HRT for post menopausal women. Larger studies are warranted to confirm these findings.

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