



Original Article

EFFECTS OF MULTIPLE MICRONUTRIENTS (MMN) ON OVULATION INDUCTION IN SUBFERTILE WOMEN WITH PCOS

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Abstract:

Introduction: PCOS is a very common disorder of reproductive women characterized by hyperandrogenism and chronic anovulation. The beneficial effects on micronutrients supplements may have been mediated not only through the presence of multiple vitamin & minerals and multiple antioxidant such as vitamin C and vitamin E. It also mediated insulin sensitization with inositol and improvement of the blood flow in the pelvic organ with the presence of L-arginine. Multiple micronutrients supplementation is a cost effective remedy that is well tolerated with no adverse effects. Its use as an adjuvant in fertility treatment may benefit women pre conceptionally.

Objective: The aims of this study was to investigate the effects of MMN in subfertile women with PCOS. And also to demonstrate that MMN is act as adjuvant therapy to a standard ovulation induction regimen. And to identify ovulation rate and pregnancy rate.

Materials and methods: This is a prospective randomized control trial. In this study total 100 patients between the age of 20-40 years were taken from infertility OPD, BSMMU and in private sector, Baridhara, Dhaka, during the period from July 2011 to June 2012. Among 100 patients 50 infertile patients undergoing ovulation

induction for 3 months were allocated to receive adjuvant MMN treated as group A. 50 infertile patient undergoing ovulation induction were not allocated to receive adjuvant treated as group B.

Results: Clinical pregnancy rate are assessed after third cycle or as soon as the women achieved pregnancy. There was no significant differences in age, menstrual history, BMI (kg/m²) in both groups. This difference was statistically significant $p < 0.04$. And also shows the endometrial thickness with TVS $> 9\text{mm}$ in 31 patients and less than 9mm in 11 patients with case group compared with the control group $> 9\text{mm}$ 11 patient and $< 9\text{mm}$ in 17 patients which is statistically significant p value < 0.05 . There was no significant difference in progesterone in both groups. There were 22 of 50 patient conceived during the study 2 miscarriage in first trimester in group A and 6 of 50 are conceived in group B and 2 miscarriage in 1st trimester. There was significant difference pregnancy rate $p < 0.001$.

Discussion: Our study is to demonstrate that multiple micronutrients supplementation is adjuvant therapy to a standard ovulation induction regimen in women undergoing treatment for anovulatory PCOS patients. The effect of this adjuvant therapy is improved the ovulation and pregnancy rate. Women who take adjuvant micronutrients supplementation during ovulation induction have a higher chance of pregnancy compared with women without micronutrients supplementation.

Conclusions: Women who take adjuvant micronutrients supplementation during ovulation induction have a higher chance of pregnancy compared with women without micronutrients supplementation.

Introduction:

PCOS is a very common disorder of reproductive women characterized by hyperandrogenism and chronic anovulation.^{1,2} It's etiology is not yet clear. Prevalence of PCOS in women of reproductive age is 5%-10% in general population. The prevalence of PCOS is 20% among infertile women. Many of this women had subtle endocrine abnormalities.³ The

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report by Burghen et al⁴ in 1980 showed that PCOS was associated with hyperinsulinaemia, it has become clear that this syndrome causes major metabolic as well as reproductive morbidities. In this study clinical presentation apart from menstrual dysfunction, acne, hirsutism, alopecia, infertility are more concerned. Menstrual dysfunction typically occurs in PCOS ranging from oligomenorrhoea to amenorrhoea. As a rule patient with PCOS exhibit anovulation. Even in hyperandrogenic woman with regular menstrual cycle, the rate of anovulation is about 20%.⁵ Approximately 50-70% of patients with PCOS demonstrate profound Insulin resistance and secondary hyperinsulinaemia. Overall Insulin resistance and secondary hyperinsulinaemia are independent of body weight. Insulin resistance and secondary hyperinsulinaemia affects a large fraction of patients with PCOS and may cause or augment the androgen excess and chronic anovulation, when compared with levels found in normal woman.⁶ Patients with persistent anovulation have higher mean concentration of LH but low or normal levels of FSH. The beneficial effects on micronutrients supplements may have been mediated not only through the presence of multiple vitamin, minerals and multiple antioxidant such as vitamin C and vitamin E, it also mediated insulin sensitization with inositol and improved blood flow in the pelvic organ with the presence of L-arginine.⁷ Multiple micronutrients supplementation is a cost effective remedy that is well tolerated with no adverse effects. Its use as an adjuvant in fertility treatment may benefit women pre conceptionally. It promotes ovulation, balances the hormone, reduces the oxidative stress, also regulates menstrual cycle, reduces in incidence of recurrent miscarriage and birth defects. It also improves the fertility rate.⁸ Those women susceptible to micronutrient deficiencies should be supplemented by micronutrients to optimize their reproductive health. The implications of the study are potentially for reaching as they suggest multiple micronutrients supplementation improve pregnancy rates. Micronutrients are the combination of herbs amino acid, vitamins and minerals. It is an adjuvant preparation to treat female infertility. The herbal and nutritional components of micronutrients have all been selected for their roles in promoting female reproductive wellness. The effect of MMN specially the inositol on follicular development is rapid because the increased circulating concentration of E_2 .⁹

Aims:

The aims of this study is to investigate the effects of multiple micronutrients in subfertile women with PCOS. And to detect ovulation and pregnancy rate as a adjuvant therapy with ovulation induction treatment.

Materials and Methods:

This is a prospective randomized control trial. In this study total 100 patients between the age of 20-40 years were taken from infertility OPD, BSMMU and from a private hospital, Baridhara, Dhaka, during the period from July 2011 to June 2012. With the inclusion criteria infertile women undergoing ovulation induction (Who are having anovulatory cycle diagnosed by doing hormone profile & TVS) treated with clomiphene citrate and or gonadotrophin. Infertile patients with male factor infertility or having tubal block were excluded from the study.

Among 100 patients 50 infertile patients were selected for ovulation induction for 3 months who were allocated to receive adjuvant MMN treated as group A. 50 infertile patient selected ovulation induction were not allocated to receive adjuvant treated as group B.

Clinical pregnancy rate are assessed after third cycle or as soon as the women achieved pregnancy. Ovarian activity was monitored using TVS by showing ovulation follicle and endometrial thickness. Data were analyzed on the basis of the intention to treat and also on completed treatment parameters where relevant ovulatory function and pregnancy rate were compared between two groups. Statistical analysis was prepared using the SPSS of windows software. Showing the difference of pregnancy rates between two groups which was statistically significant or not.

Result:

In this study total 100 infertile patient is undergoing ovulation induction by clomiphene citrate and or gonadotrophin. Among them 50 patients were treated with MMN as a group A and 50 patient is treated with ovulation induction without adjuvant as a group B. A prospective randomized controlled trail was conducted on 100 patients. Among group A there were 50 subfertile women. Another control group B 50 subfertile women. There was no significant differences in age, menstrual history, BMI (kg/m²) in both

group. And Table II showed that the developing follicle and endometrial thickness with TVS is more case group than the control group. which is statistically

significant p value <0.05. There were 22 out of 50 patient conceived during the study and 2 miscarriage in first trimester in group A. There was significant difference in pregnancy rate and p value is <0.001. The results of this study shows that women who take adjuvant MMN supplementation during ovulation induction have higher chance of pregnancy compared with women without adjuvant.

Table- I
Clinical Data

	Group A (n=50)	Group B (n=50)	P value
Age (Mean years)	22.5	23	>.05
BMI (Mean)	28	27.1	
MH /year (mean)	4.5	4	
Primary	40 (80%)	36 (72%)	
Secondary	10 (20%)	14 (28%)	>.05

Not statistically significant. P value is >.05

Table- II
Ovulation

	Group A (n=50)	Group B (n=50)	P value
Developing follicle	42(89.36)	32(71.1%)	<0.05 ^s
Endometrial thickness			
>9mm	31(73.8%)	15(46.87%)	<0.05 ^s
<9mm	11(26.2%)	17(53.12%)	>0.05 ^{ns}

Statistically significant P value is ,<0.05

Table III
Pregnancy rate

	Group A (n=50)	Group B (n=50)	P value
Pregnancy	22(44%)	6(12%)	<0.001 ^s
Miscarriage	2(4%)	2(4%)	>0.05 ^{NS}

Statistically significant P value ,<0.001

Discussion:

This study which present a comprehensive, detailed endocrinological assessment of ovarian function in the contest of a randomized case controlled trails with MMN in women with PCOS. Our data show clear

beneficial effect of MMN treatment upon ovarian -function, and pregnancy outcome women with oligomenorrhea and PCOS. Some study have shown conflicting results with respect to changes in ovulation rate and also changes in pregnancy rate during MMN treatment.⁹⁻¹⁰

Our randomized study provides some support for this proposal, although it should be noted that ovulation was only improved in the MMN group.

Most of the discontinuation cases occurred at the early part of treatment, suggesting that women prescribed MMN should be adequately counseled and perhaps actively supported through this stage.

A number of small randomized studies have shown that women with PCOS respond to this therapy increasing a ovarian activity and menstrual frequency.^{8,10} However the relationships among treatment outcome, clinical changes, glycemic, metabolic and lipid profile adjustment are not studied and remain disputed. In particular direct assessment of follicular development and endometrial thickness, the latter point is relevant because in women with PCOS may got ovulation.^{1,2} Previously published studies¹⁰⁻¹¹ give evidence that the use of micronutrients being friendly affects embryogenesis & placentation and that the prophylactic use of micronutrients may be useful in preventing several adverse pregnancy outcomes.

Conclusion:

In conclusion, we have shown that MMN treatment increases ovulation rates in women with oligomenorrhea and PCOS. Further study with large sample size could be done to see the other beneficial effect like weight loss, increase HDL and decrease cholesterol level.

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