DISCUSSION

The present comparative study was planned with an aim to find out best therapeutic approach in migraine without aura and related some mood disorders among conventional medical therapy, homeopathic therapy, conventional medical therapy combined with yoga, homeopathy combined with yoga and yoga therapy alone, most common and popular therapeutic modes in India, later, effect of yoga therapy part alone was excluded from the project due to non availability of desired patients (patients were not ready to practice only yoga for the whole treatment period). It was clearly established that effect of conventional medical therapy in migraine is effective but different side effects were also well documented. Effect of homeopathy therapy in migraine was not clearly documented; Articles on the effect of combined therapy of yoga with conventional medical therapy or homeopathy were not available before or during the time of this study. Research papers on effect of yoga in migraine was also very less.

It is very well established fact that migraine mainly affects youth during their most productive age, therefore best treatment in migraine is very much needed.

Major emphasis of this study was given on treatment mode based on obtained value of selected parameters from pre and post treatment part.
Conventional medical and homeopathy physicians were responsible for their treatment model according to “International headache society” (IHS) criteria. Selected yoga was practiced in this project.

**Effect of migraine on** -

A) **Serum cortisol**

Cortisol is a steroid hormone, very specifically glucocorticoid and one of very established stress marker in human body which negatively affects immune system. It is an end product of the sympathetic system, the hypothalamic-pituitary-adrenal-cortical axis.

Cortisol is produced by the adrenal gland in the zona fasciculata, the second of three layers comprising the outer adrenal cortex. This release is controlled by the hypothalamus. The secretion of corticotropin-releasing hormone (CRH) by the hypothalamus triggers anterior pituitary secretion of adrenocorticotropic hormone (ACTH). ACTH is carried by the blood to the adrenal cortex, where it triggers glucocorticoid secretion. The amount of cortisol present in the blood undergoes diurnal variation; the level peaks in the early morning (approximately 8 am). Reference range of serum cortisol in 8 am are 5-23mcg/dL or 138-635nmol/L.

It has been documented earlier that stress was high among migraine patients.
It has been also documented that stress may lead to dilation of blood vessels in the brain of patients who are prone to headaches and, in turn, may trigger a migraine. It is also well established that stress and pain are intensely related with each other.

Blood was collected in the early morning (around 8am) from each patient. ELISA was used (by kit method) to analyze serum cortisol in our study. Our study revealed serum cortisol level was high among migraine patients; it positively correlates with other earlier studies. Group-A patients have shown serum cortisol level was not decreased significantly after treatment. Group-B, Group C and Group-D all have shown serum cortisol level was decreased significantly.

It has been observed that Group C has shown the best statistical improvement after comparing among all four groups of percentage difference of Mean ± S.D. value.

**B) Blood pressure and pulse rate**

Changes in B.P and Pulse pressure after conventional medical therapy. It has been documented that association of blood pressure with migraine is controversial. In 1913, Janeway et al. mentioned first time that migraine was common in patients with arterial hypertension and since then the relation between blood pressure and headache has been examined in many studies.
In 2005, Scher et al.\textsuperscript{41} studied 5,755 migraine patients in the Netherlands and found higher blood pressure in individuals with migraine compared to those without migraine. In other hand Gudmundsson et al.\textsuperscript{42} found that patients had higher diastolic blood pressure and lower systolic blood pressure and pulse pressure in migraine patients compared to controls. Authors who supported the positive association suggested that rennin-angiotensin system as a biological link between hypertension and CNS activities that are relevant for migraine pathogenesis.

a) Attacks of migraine without aura and higher angiotensin converting enzyme activity are more frequent in subjects with angiotensin converting enzyme DD gene.

b) Clinical trials indicated that angiotensin-converting enzyme inhibitors as captobril and angiotensin II receptor blockers as Lisinopril are effective in the prophylactic treatment of migraine. In addition to their action on angiotensin-converting system, they alter sympathetic activity, inhibit free radical activity, increase prostacyclin synthesis and block the degradation of bradykinin, encephalin and substance P. All are implicated in the pathophysiology of migraine\textsuperscript{44,45}.

Fuchs et al.\textsuperscript{47} investigated that headache and hypertension was not associated. In a randomized sample of the Vobarno population done by Muiesan et al.\textsuperscript{13}, found no differences in headache prevalence migraine
prevalence and use of analgesic drugs in the presence of headache between hypertensive and normo-tensive subjects.

There is a consensus agreement within the International Headache Society that chronic arterial hypertension of mild to moderate degree does not cause headache but this may not be the case in patients with hypertension classified at more severe stages. Severe hypertension in the setting of new acute headache may indicate a serious underlying cause and requires urgent investigation. 

The authors who found no association between migraine and arterial hypertension considered that the frequency rates of some common vascular risks (as hypertension) might be increased among patients with migraine which is also common (coincidental or chance association). Hypertension is also a common and consistent health problem in both developed and developing countries and its prevalence is currently rising steadily.

In contrary Hegan et al. and Wiehe et al. showed that migraine patients had lower values of blood pressure. Tzourio’s et al. found lower blood pressure and reduced carotid-intima media thickness (evidence of hypertension) in migraine patients.
Homeostatic process that regulates blood pressure and decreases sensitivity to pain, i.e. a phenomenon called “hypertension-associated hypalgesia” (blood pressure linked reduction in pain sensitivity).

In support:

a) An inverse relationship between blood pressure levels and sensitivity to painful stimuli extends into the normo-tensive range.\(^{60}\)

b) Low pain sensitivity has been reported in hypertensive animals and humans and in groups deemed to be at an increased risk for the development of hypertension.\(^{61-63}\).

c) Previous studies confirmed that increasing blood pressure was linked to decreasing amounts of chronic musculoskeletal pain in different parts of the body.

In 2005, Hegan et al.\(^{64}\) observed that individuals with a high blood pressure had a lower prevalence of chronic musculoskeletal complaints than individuals with a normal blood pressure.

Our study revealed that migraine patients who were included in our study have shown little high SBP, DBP, and pulse rate. Group A showed no significant result in the case of pulse rate, SBP & DBP, but Mean ± SD of SBP was increased.
Group B has shown significant reduction in SBP & pulse rate, but no significant result observed in DBP. Group C & Group-D both have shown significant reduction in SBP, DBP and pulse rate.

It has been observed that Group C has shown the best statistical improvement after comparing among all four groups of percentage difference of Mean ± S.D. value. SBP & DBP value was increased in case of Group-A.

C) Anxiety and depression

Earlier it has been documented that anxiety and stress were higher among migraine patients, while depressions status was remain low in migraine. Recent studies mentioned frequent migraine attacks were also associated with the highest risk for developing depression; both are very common mood disorders in migraine patients. High incidence of migraine and different psychiatric disorders suggests that these disorders are likely comorbid; Different patho-physiological explanations were established:

1) Potential mechanisms include dysfunction in central serotonergic availability.

2) Fluctuations in ovarian hormone levels (common in menstrual migraine in women).

3) Dysregulation of the hypothalamic-pituitary adrenal (HPA).
4) Sensitization of both sensory and effective neural network.

It was also documented a significant proportion of psychiatric disorders variance is due to shared genetic influences.\textsuperscript{115}

Recently it is established that pain is associated with anxiety and depression in all measured location and after correction of severity of anxiety and depression in migraine patients, mentioned association weakened substantially which suggests considerable part of comorbidity of migraine and other types of pain may be explained by anxiety and depression. These psychiatric disorders have a very high cost to individual and society. Hospital anxiety and depression scale $^8$ was used to analyze anxiety and depression status among migraine patients in this project. Our study also positively correlated with previous study, depression and anxiety level both were high in migraine patients. Group- A patients have shown Depression level significantly decreased after treatment, whereas anxiety status did not decrease significantly. Group-B patients have shown both anxiety and depression status decreased significantly. Group –C and Group-D both have shown significant decrease in anxiety as well as depression level after treatment. Interestingly Group C has shown the best statistical improvement after comparing among all four groups of percentage difference of Mean ± S.D. value by ANOVA.
D) Pain

Migraine pain is perhaps the most studied of the headache syndromes secondary to the high incidence and have significant effect on the quality of life of those suffering from this condition. Pathophysiology of migraine is not clear at all, few theories were explained.

**Vascular Theory**

Migraines may begin when blood vessels in the brain contract and expand inappropriately. This may start in the occipital lobe, in the back of the brain, as arteries spasm. The reduced flow of blood from the occipital lobe triggers the aura that some individuals who have migraines experience because the visual cortex is in the occipital area. When the constriction stops and the blood vessels dilate, they become too wide. The once solid walls of the blood vessels become permeable and some fluid leaks out. This leakage is recognized by pain receptors in the blood vessels of surrounding tissue. In response, the body supplies the area with chemicals which cause inflammation and pain.

**Neural theory**

When certain nerves or an area in the brain stem become irritated, a migraine begins. In response to the irritation, the body releases chemicals which cause inflammation of the blood vessels. These chemicals cause further irritation of the nerves and blood vessels and results in pain. Substance P is one of the
substances released with first irritation. Pain then increases because substance P aids in sending pain signals to the brain.\textsuperscript{2,16}

**The trigeminovascular system in migraine**

Activation of cells in the trigeminal nucleus caudalis in the medulla (a pain-processing center for the head and face region) results in the release of vasoactive neuropeptides, including substance P and calcitonin gene-related peptide, at vascular terminations of the trigeminal nerve. These peptide neurotransmitters have been proposed to induce a sterile inflammation that activates trigeminal nociceptive afferents originating on the vessel wall, further contributing to the production of pain.\textsuperscript{2}

Recent in-vitro/in-vivo data demonstrated presence and action of prostaglandins within the trigeminal pain pathways. Migraine induction after intravenous administration of PGE\textsubscript{2} and PGI\textsubscript{2} suggests a specific blockade of their receptors, EP and IP respectively, as a new potential drug target for the acute treatment of migraine.\textsuperscript{20}

Different biologic, pharmacologic, and genetic evidence supports significant role of alterations of sympathetic nervous system, dopamine and serotonin in the Pathophysiology of migraine. CACNL1A4 gene is also may play a role in calcium-induced neurotransmitter release and/or contraction of smooth muscle.\textsuperscript{2,16}
A short form of McGill pain questionnaire was used to assess the pain intensity.

Our study documented increased pain intensity in migraine. Group-A patients have shown significant decrease in pain intensity in different segment of McGill questionnaire after treatment. Group-B patients did not show any significant improvement in migraine pain status in any segment of this pain questionnaire. Group–C and Group-D both have shown remarkable improvement in pain status in all segment of questionnaire after treatment. Group–C developed most improvement in migraine pain status after comparing with other three treatment mode by using ANOVA. Group B patients have shown slight increase Affective pain rating index in percentage difference of Mean ± S.D. value.

E) Sleep

Migraineurs reported more insomnia and other sleep-related symptoms. There are evidences which showed migraineurs on the average suffer from a relative sleep deprivation and need more sleep than healthy controls. Lack of adequate rest might be an attack-precipitating- and hyperalgesia-inducing factor.

There were evidences mentioned sleep and trigeminal pain share several common pathways with respect to neurotransmission and functions of
distinct brain areas. The role of brain stem and midbrain regions are involved. orexinergic neurons originates from hypothalamus. These neurons project to the periaqueductal grey and these are probably the anatomic and physiological link between headache and sleep. Another relevant system for this interrelationship is the melatonin metabolism. However, basic research in this field is still very preliminary and a holistic hypothesis on how sleep physiology impacts headache and vice versa is still not clear.\textsuperscript{117}

Pittsburg sleep questionnaire \textsuperscript{111,112} was used in this study to analyze sleep status. A PSQI global score >5 is considered to be suggestive of significant sleep disturbance. Our study strongly correlates with previous studies; it has observed sleep disturbances are high in migraine patients in this study.

Group-A patients did not show any significant improvement in sleep status. In other side Group-B, Group –C and Group-D established remarkable improvement in sleep status after treatment. It was also revealed that Group –C developed most improvement in sleep status in migraine pain after comparing all four post treatment group by using ANOVA.

**F) The migraine disability assessment** \textsuperscript{113}

Migraine disability assessment score defined as the consequences of illness on the ability to work and function, is measured using the Migraine Disability Assessment Score (MIDAS) used in this study. Different
evidences proved that there was loss of ability to work in migraine patients, which positively correlates with our study. \(^{(111)}\). Group-A, Group-B, Group-C and Group-D all four groups established statistical improvement in migraine disability status after treatment. It is also revealed that Group –C (Treated with conventional medical therapy combined with yoga) showed most improvement in MIDAS status.

G) Migraine Frequency and Duration\(^8\)

It has been observed that migraine characterized by paroxysmal episodes of headache and associated symptoms typically lasting four to seventy two hours\(^{(4)}\).

Evidences proved that average duration of headache phase (in hour) as well as frequency of headache days rises up along with the severity of migraine\(^{(8)}\).

Group-A, Group-B, Group –C and Group-D all four groups established significant improvement in migraine disability status after treatment. It was also revealed that Group –C (Treated with conventional medical therapy combined with yoga) showed most favorable significant result in frequency and duration of migraine attack after comparing among four groups.

- **Effect of conventional medical therapy in Migraine**

It has been observed that Group-A patients were significantly improved in pain status, Frequency and duration of migraine pain attack, migraine
disability assessment as well as depression status, but failed to establish significant improvement in Cortisol level, SBP, DBP, Pulse rate, Sleep status and anxiety level. This may be due to common drugs used to treat migraine have been associated with numerous undesirable side effects, (already discussed under Review of literature section in conventional medical therapy in migraine part).

Conventional medical therapy is very effective for migraine pain, frequency and duration but it is not so effective in treating migraine related some mood disorder i.e. Stress hormone level, sleep status, sleep and anxiety status management, which are established associated disorders.

- **Effect of Homeopathy in Migraine**

  Group –B patients were treated with homeopathy, it has been reveled that they established significant improvement in cortisol level, SBP, DBP, Pulse rate, Anxiety, depression status, Frequency, Duration of migraine and migraine assessment parameters, but failed to improve all pain parameters used in this study. Homeopathy deals with the principle of individualization. It treats the man, rather than the disease \(^{86}\). Our study is suggested that Homeopathy failed to show its impact on migraine pain within our study period (six months), but showed definitely good impact on other associated parameters, Long term study is needed to analyze the effect homeopathy in
migraine, as the concept of the treatment mode differs from conventional medical therapy.

- **Effect of yogic practice in migraine**

A number of earlier research works for the treatment of migraine pain using yoga and a number of asanas for shoulder back and neck, Pranayam showed beneficial effects. The main mechanism contributing in the yogic treatment of migraine is a state of calm alertness, which includes increased parasympathetic activity, calming of stress response systems and involvement of neuroendocrine system by releasing of hormones, also a positive coordination with thalamic generators.

Drugs used to treat that migraine have been associated with numerous undesirable side effects. Considering the yogic exercise and meditation, moderately intense aerobic exercise is well known to lower blood pressure. A very interesting finding demonstrated in a randomized controlled study showed that even a relatively short period of regular one hour yogic practice can be compared as effective method as medical therapy in controlling blood pressure of hypertensive individuals. The probable mechanism which reduces blood pressure may be due to autonomic influences, as in essential hypertension impaired baroreflex sensitivity is considered as one of the major contributing factors, so blood pressure reduction in yoga practice can be explained by its advantageous effects on autonomic neurological function.
Some researchers documented that yogic postures can restore baroreflex sensitivity. Asana that are equivalent to head up or head down tilt were the most beneficial in this context. Scientific evidences proved immediate down regulating effect of yoga on the HPA axis response to stress.

Stress management is also very well established. Yoga has an immediate quieting effect on the HPA axis to response to stress. Some studies has been hypothesized that specific yoga exercise cause a shift towards parasympathetic nerve nervous system dominance by direct vagal stimulation. Apart from the pathophysiological aspects yoga has been shown to have immediate psychological effects for decreasing anxiety and an increased emotional feeling and spiritual well being. A Questionnaire based study showed that participation in a two month yoga class can led to significant decrease in perceive levels of anxiety among females.\textsuperscript{114}Sushil et al stated that kapalbhati and breath awareness can improve the stress status,\textsuperscript{8} John et al have describe effectiveness of yoga therapy in the treatment of migraine without aura .Yoga was found to have a beneficial effect on various migraine Pain parameters.\textsuperscript{8}

Combined treatment of yoga with conventional medical therapy and Homeopathy both have shown improvement in each parameters, measured in the study, But Group –C has shown best improvement in almost each and every parameter considered in this study after comparing by ANOVA.
SUMMARY AND CONCLUSIONS

INTRODUCTION

Migraine is a common disabling primary headache disorder mainly affects youth during their most productive age. Despite the need for a perfect treatment of this debilitating condition, the ideal “cure” is yet to be established. Conventional medical therapy is effective, but it has different side effects. Alternative medicine researches are still in progress. Integrated therapy of conventional medicine and yoga may prove to be effective against migraine.

Yoga has already proved effective and popular as a therapeutic intervention in a variety of disorders and stress management, but relatively fewer articles are available on yoga in the treatment of migraine.

Homeopathy medicine practice is popular in India, Migraine management has already been adopted by homeopathy medicine. Research articles of homeopathy in the treatment of migraine are very less, as well as controversial.

Aim of the study was to find out the comparison among the efficacy of conventional medical therapy, homeopathy and yoga therapy alone as well
as combined therapy of conventional medicine with yoga and combined therapy of homeopathy with yoga.

METHODOLOGY

The present study was done in the department of Physiology, Subharti medical college and hospital, Meerut. 120 patients who had complained of migraine were selected for this study screened by physician according to “International Headache society” (IHS), criteria for migraine.

Patients were obtained from Chhatrapati Sivaji Subharti Hospital, Meerut and adjoining clinics and hospital, Meerut city, Uttar Pradesh, India.

The age groups of patients were 10-55 years. Informed consent was taken from them. Five groups were prepared as follows--

a) Treated with conventional medical therapy alone-(Group-A)

b) Treated with homeopathy therapy alone- (Group-B)

c) Treated with conventional medical therapy combined with yoga- (Group-C)

d) Treated with combined homeopathy therapy combined with yoga – (Group-D)

e) Treated with Yoga therapy alone- (Group-E).
Randomly selected one twenty patients were divided into four groups, Group-E, i.e. Treated with Yoga therapy alone was discarded latter, as no patients were willing to join this group.

Standardized questionnaires of Hospital anxiety and depression scale (HADS), McGill pain questionnaire (short-form), Pittsburgh sleep quality index, The migraine disability assessment test (MIDAS) were filled for all patients for the assessment of anxiety, depression, pain, sleep and migraine status before and after treatment. They also underwent experiments like blood cortisol estimation, recorded blood pressure, pulse rate and average frequency and duration of migraine before and after treatment.

**Group-A** Patients were received conventional medical therapy from physician (prescribed by physician only) for six months.

**Group-B** Patients were received homeopath therapy according to one homeopath physician for six months.

**Group-C** Patients were received yoga therapy combined with conventional medical therapy. They received conventional medical therapy from the same physician of group A. One professional yoga expert taught integrated yoga set including yoga asana, breathing practices, Pranayam (yoga breathing), Kriya, and meditation for 5 days a week for 60 minutes.
**Group-D** Patients were received treatment from same homeopath therapist of group-B and yoga treatment from the same yoga therapist of group- C. The protocol of the study was approved by Research ethical committee of Subharti Medical College and Hospital, Meerut, U.P.

**STATISTICAL ANALYSIS**

Graph pad software was used in this study and paired t-tests were performed to compare and analyze the data between pre and post treatment subgroup of the each same group.

1. Difference between pre and post treatment group from each group was calculated, converted it into percentage value.
2. \( \frac{(\text{Pre treatment value} - \text{post treatment value})}{\text{pre treatment value}} \times 100 \) formula was used to calculate percentage difference. All the negative sign was ignored.
3. All the percentage value of each group was compared by using one way ANOVA.
CONCLUSIONS

A) The prevalence of migraine was found to be higher in age group of 20 to 29 years (70%), and lowest in the age group of 10-19 years. Youths are mostly vulnerable in this context.

B) Women are more sufferer compare to male patients of migraine, 67% patients were women in our study.

C) Post treatment of Group-C and D have shown significant decrease in systolic blood pressure, diastolic blood pressure and pulse rate, where Group-A did not show any significant result, SBP and pulse rate status was statistically decreased in Group-B, but DBP remain unchanged in post treatment group. SBP, DBP and pulse rate were high in case of all pre treatment groups except Group-A showed statistical insignificant increase in SBP in post treatment group. Group-C developed most statistical significant change in SBP, DBP & pulse status.

D) Post treatment Group-B, C and D all have shown favorable statistical change in serum cortisol level, Group-A has not shown any significant result. Group-C developed most statistical significant change in cortisol status. Cortisol level was high in case of all pre treatment groups compared to post treatment group.
E) A significant decrease in anxiety and depression status was observed in all three Group-B, C&D, Group-A has not shown significant alternation in anxiety status but developed favorable result in depression status. Group-C developed most statistical significant change in anxiety as well as depression status. Anxiety& depression status were high in case of all pre treatment groups compared to post treatment group.

F) Group-A, C and D have shown remarkable significant decrease in all pain status Where as Group-B has not shown significant improvement in pain status of migraine, It has observed that A-PRI status was even high in post treatment group of Group-B. Group-C developed most statistical significant change in pain status. Pain status was high in case of all pre treatment groups compared to post treatment group.

G) Our study revealed women migraine patients were suffering more from disturbed sleep status(65%) compared to male patients(35%). Favorable changes have been observed in Group-B.C, and D where as group-A has not shown any statistical changes in sleep status among migraine patients after treatment. Group –C (Treated with conventional medical therapy combined with yoga) developed most improvement in sleep status in migraine pain after comparing all four post treatment group by using ANOVA. Disturbed sleep status was high in case of all pre treatment groups compared to post treatment group.
H) All four Groups have shown significant decrease in migraine disability

I) Assessment, Group-C post treatment group revealed most significant result compare to other three groups. MIDAS status was high in case of all pre treatment groups compared to post treatment group.

J) Group-A, B, C and D all have shown statistical significant result in frequency and duration of migraine attack. Group-C developed most favorable result after comparing all four groups. Frequency and Duration of migraine were high in case of all pre treatment groups compared to post treatment group.
In summary the present study evaluated the effectiveness of few commonly practiced treatment mode as well as combined treatment approach in the treatment of migraine, this present study provides preliminary evidences that integrated yoga therapy combined with conventional medicine may be used together as an effective treatment mode in migraine and related mood disorders. However further long term studies are required in more depth to ascertain more beneficial effects.

Limitations of this Study

The main drawback of the study is limited number of sample size, and recommended to perform a multicenter study in future with a larger population, Long term follow up as well as neuro-physiological study is also needed to get more accurate results.