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A clinical evaluation of Siddha herbal formulation *Panchathaarai kuzhambu* (Internal medicine) and *Ottrai thalaivali thylam* (External medicine) in the management of *Ottrai thalaivali* (Migraine)

Research Article

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Abstract

Migraine is a syndrome of headache which is benign and re-occurring, along with various neurological dysfunctions, nausea/vomiting etc, affecting about 20% of females and 6% of males at some point in life. It affects over one billion people worldwide. According to Siddha, *Ottrai thalaivali* (migraine) is characterized as unilateral headache, lacrimation, irritability, sighing, fatigue, tremor, startling, loss of appetite and tingling sensation. Research studies regarding Migraine was searched in databases like PubMed, Google scholar, scopus, web of science, using keywords Migraine and siddha, Migraine AND *Panchathaarai kuzhambu, Ottrai thalaivali* and Clinical trial. Eventhough, there are a few papers proving the effectiveness of ayurvedic treatment regimens for migraine, no works have been found relating siddha clinical trials and migraine. Also, as the disease requires long term management, there is a need to look for herbal formulations that can be effective in the management of Migraine. The herbal formulations *Panchathaarai kuzhambu* and *Ottrai thalaivali thylam* have been taken for the study to prove its effectiveness on Migraine. A Clinical trial was conducted on 10 patients diagnosed with *Ottrai thalaivali(Migraine*). The trial drugs *Panchathaarai kuzhambu* was given in a dose of 2gms twice daily along with cow's milk and *Ottrai thalaivali,* 70ml as bath oil twice in a week, given for 48 days. The results using HIT-6 Score and Headache diary showed that there was significant relief in the patients and there was no untoward side-effects in any patients.

Keywords: *Panchathaarai kuzhambu,* HIT-6 score, Migraine, *Siddha, Ottrai thalaivali thylam,* Headache diary.

Introduction

One billion people worldwide have been affected by Migraine(1) and the observed prevalence (one year) of migraine was 63.9% in Southern India (the mean global prevalence is estimated at 14.7%)(1). It is the second most common disabling condition worldwide. Migraine is a syndrome of headache which is benign and re-occurring, along with various neurological dysfunctions, nausea/vomiting etc(2), affecting about 20% of females and 6% of males at some point in life(3).

Migraine is a disorder characterised by episodes of mild to moderate unilateral form of headache, generally associated with nausea/vomiting, sensitivity to light and sound. Migraine is a French word, owing its origin to a Greek word, 'Hemi crania' meaning half of the head, which is also called 'Hemigranea' in Latin(4). Migraine is a very important issue as co morbidity; Chronic Migraine is co morbid mostly with psychiatric disorders, sleep disorders, cardiovascular disease. Stroke, Epilepsy, fibromyalgia and fatigue(5) also has migraine co-morbidity. It impacts the quality of life due to severe pain and requires long-term management.

In Siddha, diseases of Mankind are listed as 4448 in number. Among them, *Oru thalai vaadham (ottrai thalaivali)* is one of the 80 *Vatha* diseases (diseases due to vitiation of *vatha* humour) which is correlated with Migraine headache in modern science(7). The siddha text, *Chikitsa rathna deepam* has explained, *Ottrai thalaivali* as syndrome of unilateral headache, lacrimation, irritability, sighing, fatigue, tremor, startling, loss of appetite and tingling sensation(6). The causative factors of the symptoms of migraine involve the vitiation of pitha, vatha in the place of kabha and abnormal functioning of *udhana, vyanan, samana, koorman and kiruharan, of vatha* (divisions of *vatha* humour), *saathagam* and *aalosakam* in *pitha*(divisions of *pitha* humour), *avalambagam* and *tharpagam* in *kabha* (divisions of *kabha* humour).

Research studies regarding Migraine was searched in databases like PubMed, Google scholar, scopus, web of science, using keywords Migraine and siddha, Migraine AND *Panchathaarai kuzhambu, Ottrai thalaivali* and Clinical trial. Eventhough, there are a few papers proving the effectiveness of ayurvedic treatment regimens for migraine, No works have been found relating siddha clinical trials and migraine. Also as the disease requires long term management, there is a need to look for herbal formulations that can be effective in the management of Migraine.

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The aim of the study is to evaluate the therapeutic effectiveness of the internal medicine, *panchathaarai kuzhambu* and external medicine *ottrai thalaivali thylam* in the management *ottrai thalaivali* (migraine) through headache impact test score(20). Also, Determination of headache frequency, duration of headache, intensity of headache, preceding symptoms, nature of headache, associated symptoms, suspected triggers and relief through headache diary(21).

Materials and methods

Selection of drugs

The *siddha* herbal formulations selected for the present study are *Panchathaarai kuzhambu* given its ingredients in *table1,* and *Ottrai thalaivali thylam* give its ingredients in *table 2.* These are sastric preparations taken from classical texts, *Agathiyar vaithya kaviyam 1500* and *Aathmarakshamirtham enum vaithya saara sangraham* respectively mentioned for the treatment of *Ottrai thalaivali (Migraine).*The five raw drugs (purified) mentioned in the *table-1*, was taken and finely powdered as per SOP mentioned for *chooranam*(fine powder form), then the prepared *chooranam* (fine powder form) was stored in a dry airtight container. The first three raw drugs (purified) mentioned in the *table-2* are powdered well and is mixed to the gingelly oil, then the mixture was boiled till the colour of the oil got red. Then the oil was allowed to cool and was stored in a dry airtight glass container.

Table 1: Ingredients of Panchathaarai kuzhambu

S.no	Common name	Botanical name	Quantity
1.	*Naatu chakarai*	*Saccharam officinarum.Linn*	*4 kazhanju (20.4g)*
2.	*Chukku (Dried ginger)*	*Zingiber officinale.Roscoe*	*3 kazhanju (15.3g)*
3.	*Injii (Ginger)*	*Zingiber officinale.Roscoe*	*2 kazhanju (10.2g)*
4.	*Thipilli*	*Piper longum.L*	*2 kazhanju (10.2g)*
5.	*Elam*	*Eletaria cardamomum, Maton*	*1 kazhanju (5.1g)*

Table 2: Ingredients of ottrai thalaivali thylam

S.no	Common name	Botanical name	Quantity
1.	*Athimathuram*	*Glycyrrhiza glabra.Linn*	*2balam(70g)*
2.	*Chukku*	*Zingiber officinale.Roscoe*	*2balam(70g)*
3.	*Vasambu*	*Acorus calamus,Linn*	*2balam(70g)*
4.	*Nallennai*	*Sesamum indicum, Linn*	*1padi(1300ml)*

An open clinical trial was conducted after getting Institutional Ethical committee clearance dated, 22/12/2022: NIS/23/IEC/2022/MP/6 and CTRI registration with registration number CTRI/ 2023/02/049693. The study was done with a total of 10 patients selected by an inclusion criteria of age limit within 18-65 years, and having five migraine attacks, in the last 3 months each lasting for 4-72 hours and having any two of the following characteristics , unilateral type of headache, pulsating quality, mild to moderate intensity, aggravation by routine physical activity, often accompanied by nausea (and/or vomiting) or sensitivity to light and sound(2), Headache Impact Test total score(20) range 36-59 was included. Patients with Cervical spondylosis, cerebro vascular diseases, trigeminal neuralgia, traumatic history, psychiatric illness, seizures, alcoholism, sinusitis headaches, ear disorders, eye diseases, diabetes mellitus, hypertension, patient with any other serious systemic diseases were excluded.

The internal medicine, *Panchathaarai kuzhambu* was given in a dosage of 2 g (twice a day, AF) with cow's milk, the external medicine, *ottrai thalaivali thylam* was given in a dosage of 70ml for oil bath twice in a week, both for a duration of 48 days. The enrolled patients visited the hospital once in a week. Clinical assessment was done at each visit and prognosis was noted. Clinical symptoms, Headache impact test score, and headache diary was evaluated before and after treatment. The Headache impact test score contains six items in a questionnaire that measures the adverse impact and severity of headache. HIT-6 Score is a reliable and valid tool utilised in clinical practice and many clinical trials(20). The results of the score comes in 4 severity categories namely; little or no impact (49 or less), some impact (50-55), substantial impact(56-59), and severe impact (60-78). Reduction of score before and after treatment from severe category to substantial or some or little impact categories is considered as an improvement(20). Headache diary is a subjective assessment to track headache characteristics. such as: duration, frequency, intensity, triggers, and relief. This is a slightly modified form of the National Headache Foundation's Headache diary.The method of assessment of the headache diary before and after treatment was as follows: Duration was assessed based on the maximum hours of an migraine episode in patients. The results were in 4 categories: 4-20hrs, 21-37hrs, 38-54 hrs, 55-72 hrs (migraine headache can range from 4-72 hrs)(2), frequency of headache was assessed based on how frequent was the migraine episodes and the result was recorded as high, moderate, low, and very low categories, intensity was assessed as the severity of headache felt by the patients before and after treatment (rate1-10), Preceding symptoms was recorded as whether any symptoms where present or not before the episode of headache. Triggers of headache as mentioned by the patients were recorded as stress, sleep pattern, sun exposure, travel, food. Relief of headache was recorded based on whether the relief felt by the patients after taking medication was complete or moderate or no relief(21) .The results of the HIT-6 score

was statistically analysed using Wilcoxon signed rank method, Headache diary was statistically analysed using Wilcoxon signed rank and Mcnemar test.

Observation and results

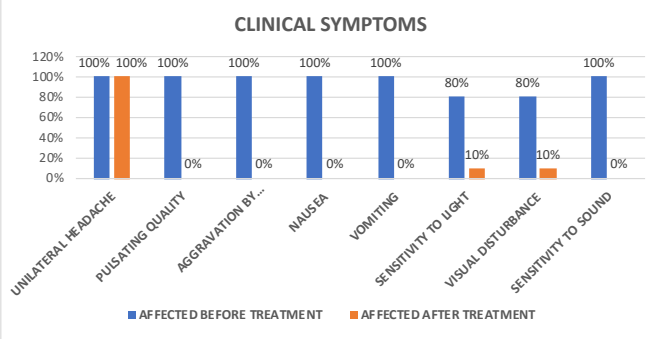
Out of 10 patients, 7 patients were male, 3 patients female, 8 patients were of mixed diet, 7 patients had the habit of drinking tea, 9 patients were married, most of the patients were of office work, and 5 patients had family history of Migraine. *Thega ilakanam* (body constitution) of the patients were mostly *pithavatham* and *pithakabham*. *Rasogunam* (character)was observed in most of the patients, *naadi* (pulse) was observed to be *vathapitham*, and *pithavatham* in the patients.

Before treatment, all the 10 patients (100%) had symptoms of unilateral pain, pulsating quality, aggravation by activity, nausea, vomiting, sensitivity to sound. Sensitivity to light and visual disturbance was seen in 8 cases(80%). After treatment, Unilateral pattern of pain had no change, there was improvement in the symptoms of pulsating quality, aggravation by activity, nausea, vomiting, sensitivity to sound in all 10 patients(100%). Sensitivity to light and visual disturbance was improved in 7 patients(70%) of the cases*(table 3)(fig 1)*.

Table 3: Showing the results of clinical symptoms obtained

Clinical symptoms	No . of .patients (percentage)	
	Affected before treatment	Affected after treatment
Unilateral headache	100%	100%
Pulsating quality	100%	0%
Aggravation by physical activity	100%	0%
Nausea	100%	0%
Vomiting	100%	0%
Sensitivity to light	80%	10%
Visual disturbance	80%	10%
Sensitivity to sound	100%	0%

Fig 1: Changes in clinical symptoms before and after treatment



The Headache impact test score(20) contains six items in a questionnaire that measures the adverse impact and severity of headache. HIT-6 Score is a reliable and valid tool utilized in clinical practice and many clinical trials. The results of the score comes in 4 severity categories namely; little or no impact (49 or less), some impact (50-55), substantial impact(56-59), and severe impct (60-78). Reduction of score before and after treatment from severe category to substantial or some or little impact categories is considered as an improvement(20).HIT-6 Scores(20) were reduced after treatment for all the patients. The highest reduction score was 46 and the lowest reduction score was 40. Before treatment, All the 10 patients had their HIT-6 scores(20) between 56-59 showing that the patients had moderate impact of headache. After treatment, HIT-6 scores(20) were reduced in all the 10 patients between 36-49 showing that the patients had reduced from moderate to little impact of headache *(table 4) (fig 2)*.

Table 4: Headache impact test score before and after treatment

S no	Op id	HIT-6(bf)	HIT-6(af)
I	213758	57	42
2	96547	58	44
3	662045	59	46
4	93624	56	46
5	85863	59	43
6	475528	59	46
7	94971	59	40
8	65855	58	46
9	89800	58	42
10	84010	59	40

Fig 2: Headache impact test score before and after treatment

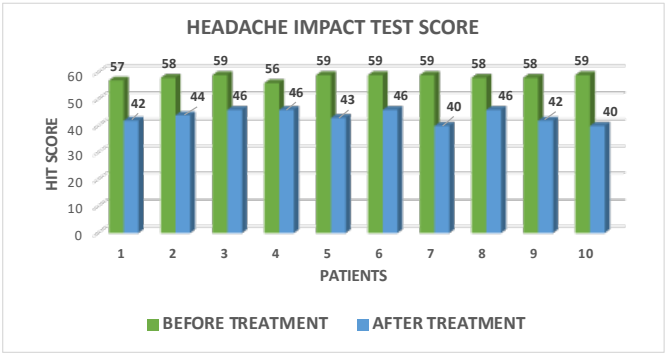
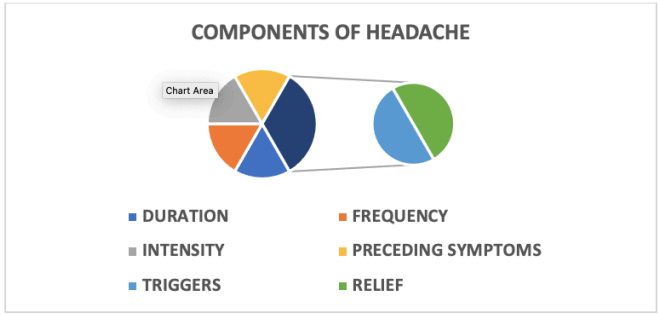


Fig 3: Components of Headache Diary



Headache diary(21), is a subjective assessment tool recorded by the patient during a treatment period. Duration was assessed based on the difference in the maximum hours of an migraine episode in patients, before and after treatment. There results were in 4 categories: 4-20hrs, 21-37hrs, 38-54 hrs, 55-72 hrs (migraine headache can range from 4-72 hrs)(2),Before treatment, duration of headache was 21-37 hrs in 5 patients, 2 patients had headache of 38-54 hrs, 3 patients had headache of 55-72 hrs. After treatment, all the 10 patients had reduction in duration of headache, to 4-20 hrs *(fig 4)*. Frequency of headache was assessed based on how frequent was the migraine episodes and the result was recorded as high, moderate, low, and very low categories,Frequency of headache in 5 patients (50%) was high, 5 patients (50%) was moderate form of headache. After treatment, there is moderate reduction of frequency in 8 patients (80%) and low frequency in 2 patients *(fig 5)*. Intensity was assessed as the difference in severity of headache felt by the patients before and after treatment (rate1-10) was recorded Out of 10 patients, 5 patients had 10 as their intensity of headache score, 2 patients had 9 as their intensity score, 3 patients had 8 as their intensity score. After treatment, 3 patients (30%) had 5 as their intensity score, 3 patients (30%) had 4 as their intensity score, 2 patients (20%) had 3 as their intensity score, and 2 patients (20%) had 2 as their intensity score *(fig 6)*. Preceding symptoms was recorded as whether any symptoms where present or not before the episode of headache. Out of 10 patients, 6 patients (60%) had preceding symptoms before headache, which remained the same before and after treatment. Triggers of headache as mentioned by the patients were recorded as stress, sleep pattern, sun exposure, travel, food. Out of 10 patients, 3 patients(30%) had stress as their trigger factor, 3 patients(30%) had sleep pattern as their trigger factor, 2 patients (20%) had sun exposure as trigger, 1 patient (10%) had travel as trigger factor, and 1 patient (10%) had food as trigger factor, which remained the same before and after treatment *(fig 7)*. After treatment, there was moderate relief of headache in all the 10 patients(100%) *(fig 8)*. This was a subjective assessment that was recorded based on whether the relief felt by the patients after taking medication was complete, moderate or no relief.

Fig 4: Changes in duration of headache before and after treatment

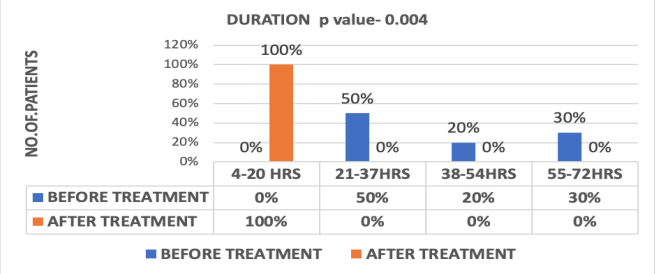


Fig 5: Changes in frequency of headache before and after treatment

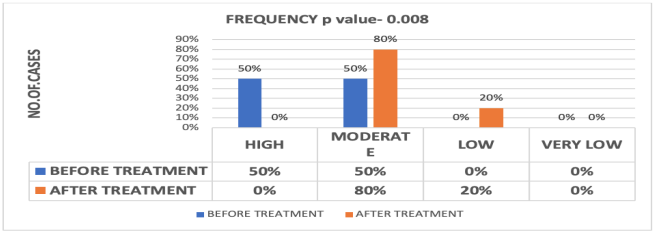


Fig 6: Changes in intensity of headache before and after treatment

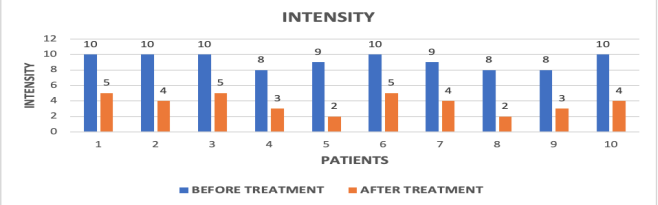


Fig 7: Triggers observed in patients in percentage

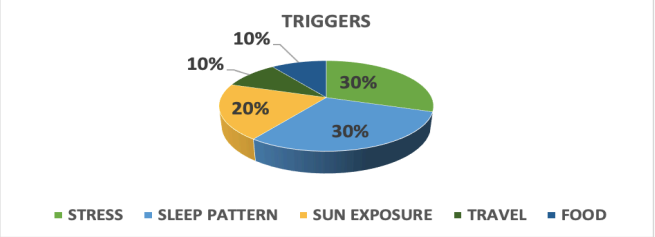


Fig 8: Relief of headache felt before and after treatment

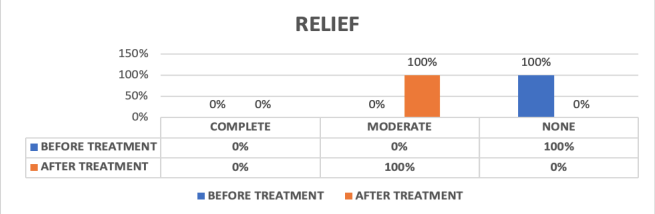


Table 5: Statistical analysis of HIT-6 Score

Wilcoxon signed rank test						
HIT-6 score		**N**	**Mean rank**	**Sum of ranks**	**p-value**	**Inference**
HIT (after-before)	Negative ranks	10	5.50	55.00	0.005	Statistically significant
	Positive ranks	0	0.00	0.00		
	Ties	0				
	Total	10				

Table 6: Statistical analysis of Headache Diary

Wilcoxon signed rank test						
Headache diary		**N**	**Mean value**	**Sum of ranks**	**p value**	**Inference**
Duration (after-before)	Negative ranks	10	5.50	55.00	0.004	Statistically significant
	Positive ranks	0	0.00	0.00		
	Ties	0				
	Total	10				
Frequency (after-before)	Negative ranks	0	0.00	0.00	0.008	Statistically significant
	Positive ranks	7	4.00	28.00		
	Ties	3				
	Total	10				
Intensity (after-before)	Negative ranks	10	5.50	55.00	0.004	Statistically significant
	Positive ranks	0	0.00	0.00		
	Ties	0				
	Total	10				
Triggers (after-before)	Negative ranks	0	0.00	0.00	1.000	Not Statistically significant
	Positive ranks	0	0.00	0.00		
	Ties	10				
	Total	10				
Relief (after-before)	Negative ranks	10	5.50	55.00	0.002	Statistically significant
	Positive ranks	0	0.00	0.00		
	Ties	0				
	Total	10				

Discussion

In this study, most of the patients were of mixed diet and had a habit of drinking tea, showing that dietary habits has a significance in migraine episodes as mentioned in previous research works(16). Stress is a known trigger for migraine(17). Common sources of stress, such as office work and marital responsibilities can contribute to the frequency of headaches. Our patient population reflected this trend with most patients being office workers and married. Half of the patients had family history of migraine that correlates with the previous studies. This reinforces the importance of considering genetic factors in the diagnosis of migraine(18). As migraine is a *pitha vatha* disease, and the *naadi*, *thega ilakanam* observed in most of the patients were related to *pitha*, migraine can be considered as a type of *pitha vatha* diseases. From the reduction of clinical symptoms, reduction in HIT-6 score and changes in headache diary before and after treatment as shown in this study, there is a an evident hope for migraine patients to have a better life with siddha treatment. No adverse drug reactions were observed during the course of this treatment. *Panchathaarai kuzhambu* is a simple polyheral formulation in the form of *chooranam* that is indicated for all forms of headache, nausea and deranged Pitham. According to siddha, the ingredients *Chukku, Injii, Elam* has hot potency due to its pungent taste, whereas *Thipilii and Panchathaarai (*palm jaggery) has cool potency due to its sweet taste(19). The ratio of the pungent drugs and sweet drugs is 1:1 making it a *samaseedhaushnam(*equalises hot and cold potency) drug. Being a *Samaseedhaushnam* formulation, when given in cow's milk (sweet) it can easily pacify the deranged *Pitham*, without increasing/disturbing *kabham* and *vatham*. This makes the drug an effective choice for working in the place of *kabha (head)* by pacifying the deranged *kuttrams*. Each ingredient of this formulation had been proven to have phytochemicals and activities that acts on the central nervous system and digestive tract. Activities of the individual ingredients like Antioxidants(11), anti-inflammatory(10), antinociceptive(9), vasculo-protective(11), analgesic (12), antidepressants(13), anticonvulsants(14), sedatives(15) works well in migraine, tension headaches, and other secondary forms of headache.Therefore, the trial drug has taste and potency that can pacify *pitha* and balances deranged *kuttrams* in the place of *kabha* which is head. This drug could work effectively in the central nervous system and can reduce stress, and headache.The statistical analysis shows significant results proving that the drug can be used in the effective management of migraine headache.

Conclusion

The results of this clinical trial from HIT-6 Score and headache diary shows that the trial drugs are clinically effective in treating migraine headache. As the ingredients are purely herbal, having known properties to relieve headache, it can be concluded that, the herbal formulations *Panchathaarai kuzhambu* and *Ottrai thalaivali thylam* can be significantly effective in the

long term management of migraine headache. The sample size being very less, the study may be done with same medicines in a larger population for further evaluation.

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