

## Clinical trials in the management of migraine carried out at IPGTRA, Jamnagar: A review

Kumari Archana<sup>1</sup>, DB Vaghela<sup>2</sup>

<sup>1</sup> Ph.D. Scholar, Department of Shalaky Tantra, ITRA, Gujarat Ayurved University, Jamnagar, India

<sup>2</sup> Professor and Head, Department of Shalaky Tantra, ITRA, Gujarat Ayurved University, Jamnagar, India

### Abstract

**Background:** Migraine is a painful episodic neurovascular disorder with recurrent attacks of headache that are typically throbbing and unilateral/bilateral and often mild/severe. The events of attacks are usually escorted by cardinal features such as nausea, vomiting and aversion to multiple stimuli like sound, light and smell, prevail for almost 4 to 72 hours, may or may not lead by focal neurological phenomenon. These cardinal features are classified in *Ayurveda* under *Shiro Roga* (head diseases). All kind of *Shirah Shoola* are broadly termed as *Shiro Roga*.

**Objective:** To review research work carried out in Shalaky Tantra department in the management of Migraine.

**Methods:** Research work on migraine management carried out between 2008 and 2019 has been reviewed. All studies were compared regarding methodology and results are included in this review.

**Results:** All the studies reviewed were aimed at enhancing the efficacy of Ayurvedic medicines, i.e. *Laghu Sutashekhara Rasa*, *Sutashekhara Rasa*, *Brihat Dashmoola Taila*, *Brihat Jeevakadya Taila*, *Go-Ghrita Nasya*. To date, a total of four clinical studies in the field of migraine have been conducted at the Department of Shalakyatantra, IPGT & RA, Jamnagar.

**Conclusion:** The aforesaid ayurvedic intervention carried out previously were effective not only in relieving the cardinal features but also helps in relieving constipation and acidity. Ayurvedic interventions provided better result in comparison to modern intervention and placebo.

**Keywords:** *brihat dashmoola taila*, *laghu sutashekhara rasa*, migraine, *shiro roga*, *shirah shoola*

### Introduction

Migraine is a painful neurovascular disease whose appearance results from an interplay of enviro-genomic factors and the severity of symptoms often propels migraines to abuse medication. Among the world's top 20 main causes of disability, migraine has been recognised by the World Health Organization (WHO) [1]. Migraine is estimated to account for 2.0% years of life lost due to a disability in women of all ages. In all genders of all ages, migraine is accountable for 1.4% of total years of life lost due to a disability [2]. World Health Organization classified severe migraine attacks as among the most disabling illnesses, comparable to quadriplegia, dementia and active psychosis [3]. Migraine is documented as the second leading cause of disability globally with high prevalence and as the top reason of years survived with disability in individuals aged 15 to 49 [4]. Migraine is currently rank sixth in worldwide prevalence, 15% of the inhabitants suffers migraine, and is posing a hefty burden on individuals and society [5]. Modern science enforced several medicines like anti-inflammatory, analgesics, NSAIDS etc. in the management of Migraine but still population is facing the existing gaps in the preventive and symptomatic treatment of migraine. Exposure to the causative factors (*Nidana*), *Dosha* placed in the *Shirah* (head) undergo vitiation. These vitiated *Doshas* are responsible enough to manifest *Shirah Shoola* of various kinds and intensity. All the *Shiroroga* are *Sannipatika* [6, 7] but *Acharya* classified the *Shiroroga* according to the dominant *Dosha* and one *Shiroroga* is classified on the basis of *Kshaya* (emaciated) *Dosha*. *Acharya Charaka* believed that after reaching *Shirah*, the vitiated *Doshas*, vitiate *Rakta* (*Rasavaha* and *Raktavaha*

*Srotasa*) there to create *Shiro Roga* (head diseases) [8]. The present study aims to highlight the effective role of Ayurvedic drugs, i.e. *Laghu Sutashekhara Rasa*, *Sutashekhara Rasa*, *Brihat Dashmoola Taila*, *Brihat Jeevakadya Taila*, *Go-Ghrita Nasya*.

### Materials and Methods

A systemic literature search was performed using the departmental library for research work carried between 2008 and 2018 in the management of Migraine. Total four clinical researches have been carried out in the subject of Migraine at Department of Shalaky Tantra, Institute for Post Graduate Teaching and Research in Ayurveda (IPGT & RA), Jamnagar. (Table 1).

**Table 1:** Details of Clinical Research Works on Migraine at Department of Shalaky Tantra, IPGT & RA, Jamnagar.

Study No.	Name of Researcher	Year	No. of Registered Patients
1	Hemal <i>et al.</i>	2008	44
2	Mata <i>et al.</i>	2015	30
3	Vaghela <i>et al.</i>	2015	150
4	Mata <i>et al.</i>	2018	107

All studies were compared regarding methodology and results and included in this review.

### Results

In all clinical trials, patients attended outpatients department of Shalaky department, IPGT & RA, hospital fulfilling the diagnostic criteria were selected randomly, irrespective of their caste, sex, religion, *Desha* (place), *Prakriti* (nature) etc. The informed written consent of patients was obtained

prior to starting treatment and patient information sheet were provided to the patient. Patients having signs and symptoms of migraine, age group 16-60 years were included for trial whereas patients with any chronic debilitating disease with other neurological pathologies or sinusitis, hypertension, secondary headache caused by meningitis, tumour, encephalitis, cervical spondylitis and refractive errors, age groups below 16 and above 60 were excluded from the study.

### Drugs

All Ayurvedic trial drugs were prepared in the pharmacy of Gujarat Ayurved University, Jamnagar. Pharmacognostical and analytical studies were conducted in the laboratories of IPGT & RA, Gujarat Ayurved University, Jamnagar.

### Investigations

Routine haematological, urinary and blood sugar level analyses were conducted prior to treatment to rule out any systemic disease. Digital PNS X-ray, ophthalmological fundus examination, nasal endoscopy and CT-SCAN were

Performed wherever necessary.

### Subjective Criteria

Patient improvement was assessed on the basis of relief of symptoms such as headache severity, frequency of headache, duration of headache, nausea, vomiting, aura, vertigo, associated symptoms of illness.

### Overall Assessment

An assessment scale was made to assess the rate of improvement. At the end of treatment, the results in view of percentage of relief were classified.

### Statistical Estimation of Results:

The data collected has been statistically analysed. Values were expressed as a percentage of relief and a standard error mean. The data were analysed by paired 't' test within the groups, while the unpaired 't' test was used for comparison between the groups. Details of intervention of previous four research works have been mentioned in Table 2.

**Table 2:** Details of Intervention of Four Research Works.

Study No.	Name of Researcher	No. of Groups	Details of Intervention
1	Hemal <i>et al.</i>	2	Group A: <i>Laghu Sutashekhara Rasa</i> 500 mg trice daily. (oral route) Group B: <i>Laghu Sutashekhara Rasa</i> 500 mg trice daily. (oral route) + <i>Brihat Dashamoola Taila</i> for <i>Nasya</i> (nasal route) Dose: 6-8 drops in each nostril. Procedure: 3 sittings of 7 days at the interval of 7 days. Duration: 6 week,
2	Mata <i>et al.</i>	2	Group A: <i>Sutashekhara Rasa</i> 250 mg BD + <i>Brihat Jeevakadya Taila Nasya</i> Dose: 6-8 drops in each nostril. Procedure: 2 sittings of 7 days at the interval of 15 days. Group B: Flunarizine 10 mg OD. Duration: 45 days.
3	Vaghela <i>et al.</i>	4	Group A: <i>Laghu Sutashekhara Rasa</i> 500 mg trice daily. (oral route) Group B: <i>Brihat Dashamoola Taila</i> for <i>Nasya</i> (nasal route) Dose: 6-8 drops in each nostril. Procedure: 4 sittings of 7 days at the interval of 7 days. Group C: Placebo tablet (wheat flour) 500 mg tablet trice daily. (oral route) Group D: <i>Go-Ghrita Nasya</i> (nasal route) Dose: 6-8 drops in each nostril. Procedure: 4 sittings of 7 days at the interval of 7 days. Duration: 60 Days.
4	Mata <i>et al.</i>	2	Group A: Experiment group (n=70) <i>Brihat Dashamoola Taila</i> for <i>Nasya</i> (nasal route) Dose: 6-8 drops in each nostril. Procedure: 4 sittings of 7 days at the interval of 7 days. + <i>Laghu Sutashekhara Rasa</i> , 500 mg Tablet TDS (oral administration). Group: Control group: (n=30) Flunarizine Tab 10mg, 1 tab. HS Duration: 60 days

1. Parekh Hemal (2008) in her study (n=44) reported that together with *Brihat Dashmoola Taila Nasya*, *Laghu Sutashekhara Rasa* provided better results in all chief complaints and associated complaints. Statistically significant ( $p < 0.001$ ) results were found in Group B compared to Group A i.e. *Laghu Sutashekhara Rasa* [9].
2. Mata (2015), in her study (n=30) reported that Group A, i.e. SR along with BJT *Nasya* provided better results in all chief complaints and in associated complaints. Statistically highly significant ( $p < 0.001$ ) result was found in Group A in comparison to Group B, i.e. Flunarizine [10].
3. D.B. Vaghela (2015) in his project work (n=150) reported that *Laghu Sutashekhara Rasa* is more effective than *Brihat Dashmoola Taila Nasya* and *Go Ghrita Nasya* in all chief complaints and in associated complaints. Statistically highly significant ( $p < 0.001$ ) result was found in *Laghu Sutashekhara Rasa* in comparison to other drugs [11].
4. Shweta Mata (2018) in her study (n=107) reported that in each chief complaint and the associated complaints,

*Laghu Sutashekhara Rasa and Brihat Dashmoola Taila Nasya* have given better results. In Group A, the findings of Group A were statistically significant ( $p < 0.001$ ) compared with Group B i.e. Flunarizine [12].

### Overall effect of therapy

Study 1: Marked improvement was observed in group B (52.4 %) and group a (35 %) whereas moderate improvement in group B (41 %) and group a (35 %).

Study 2: Marked improvement was observed in group a (80 %) and group B (60 %) while moderate improvement in group B (33.33 %) and group a (13.33 %).

Study 3: Moderate improvement observed in group D (48.89 %), group B (21 %) and group a (16 %) while marked improvement in group D (28.89 %), group a (36 %) and group B (16 %).

Study 4: Complete relief was observed in group a (41.43 %) and group B (43.33 %) while marked improvement in group a (52.86 %) and group B (43.33 %).

The over-all effect of therapy of above clinical trial has been summarised in Table 3.

**Table 3:** The Overall Effect of Therapy.

Assessment of Results	Study 1		Study 2		Study 3				Study 4	
	Group		Group		Group				Group	
	A	B	A	B	A	B	C	D	A	B
Complete relief (%)	5	05.88	06.67	00	38	02.23	00	2.22	41.43	43.33
Marked relief (%)	35	52.94	80	60	36	16	00	28.89	52.86	43.33
Moderate relief (%)	35	41	13.33	33.33	16	21	00	48.89	05.71	06.67
Mild relief (%)	25	00	00	25	10	07	10	20	00	06.67
No relief (%)	0	00	00	00	00	00	90	00	00	00

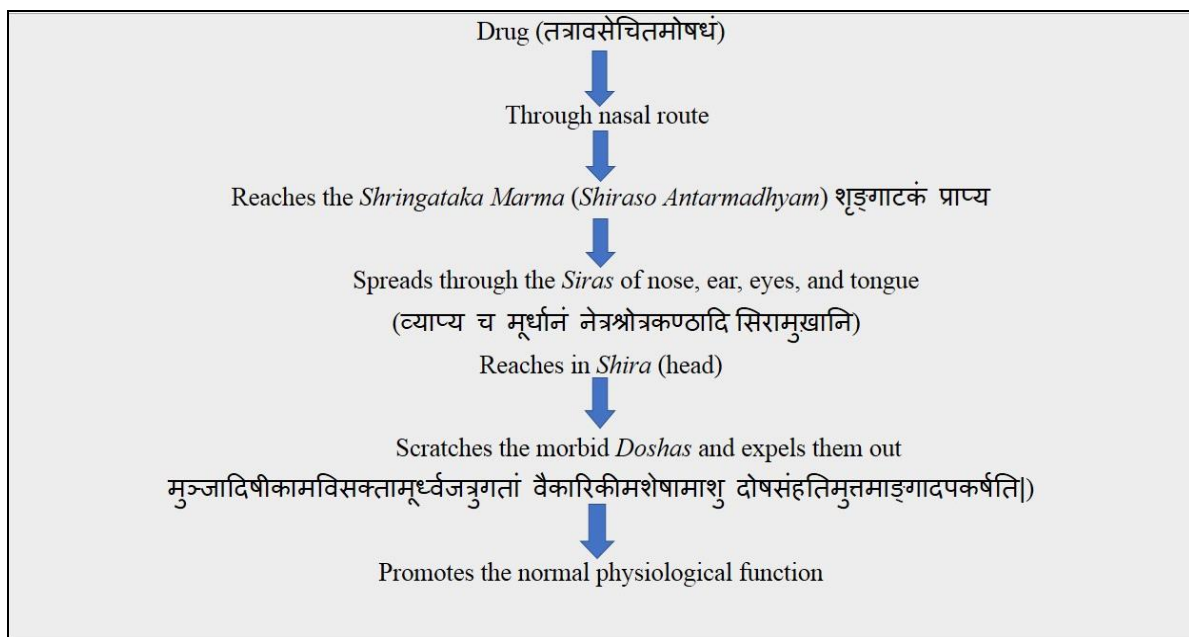
**Discussion**

The episodes of Migraine are paroxysmal in nature is explained in almost all the texts. The various types of pain explained by different *Acharyas* suggest the *Vishama* (irregular) nature of *Vata Dosha*. A total of four research studies on migraine in the department of Shalaky Tantra, IPGT & RA, Jamnagar have been conducted to date. Two research papers included *Laghu Sutashekhara Rasa* and *Brihat Dashmoola Taila*, one on *Sutashekhara Rasa* and *Brihat Jeevakadya Taila Nasya*, one on *Sutashekhara Rasa*. *Laghu Sutashekhara Rasa* and *Sutashekhara Rasa* were used for the systemic treatment of migraine in the current research. The root cause of migraine is *Agnimandya* (disrupted digestive process) in which *Kapha* vitiation occurs, and Ayurveda also suggests that *Agnimandya* is the root cause of all diseases.

Thus, if *Agnimandya* is treated, the development of *Rasa-Rakta Dhatu* (tissues) would eventually increase. By acting on *Amashaya* and *Pakvashaya*, *Sutashekhara* relives the *Amlata* and *Tikshanta* of *Pitta*. So *Pittotpati* regularises it. The contents of *Chhardi* (vomiting) and *Bhrama* (vertigo) subsides in migraine by the use of these drugs are also pacified by the driver *Dosha Vata*. Improper digestion in the intestine (*Vidagdhaejerna*) putrifies the food and produces *Ama-Visha* (toxins).

So there are *Rasa-Rakta Dusti* and *Vata* dominant *Tridosha Vikruti*. This is the basic physiology of pathophysiology behind migraine (*Shiro Roga*). For such forms of *Ama-Visha*, both *Laghu Sutashekhara Rasa* and *Sutashekhara Rasa* are the best treatment lines. Ingredients of *Laghu Sutashekhara Rasa* possess *Ushna Virya* with *Deepana – Pachana* property. The *Shlishta* morbid *Doshas* are softer and liquefied, which is ultimately removed due to the property of *Anulomana* and *Virechana Karma*, thus relieving constipation and acidity. Thus the *Pratiloma Gati* of *Vata* is prevented and *Shirah Shoola* is pacified. For the *Urdhvajatrugata Rogas* (*supraclavicular diseases*) and *shiro roga, nasya karma* is the safest cure. This is because the nose is the nearest path to the head from which the head removes morbid *Dosha*.<sup>[13]</sup> Migraine can be handled better with *Nasya* as one of the head disorders (*Shirorogas*). The only treatment that can directly affect *Pranadhistan* and *Indriya* is *Nasya*<sup>[14]</sup>. *Mriudupaka Taila form* is used for *Nasya*<sup>[15]</sup>.

This form of process is biphasic (*Mridupaka*), i.e. the aqueous soluble portion of the active concept is readily absorbed by mucosa and the soluble fat content can be readily absorbed by nerve endings. (Figure 1).



**Fig 1:** Mode of action of Nasya Karma

In study of Hemal *et al.* and Vaghela *et al.* *Brihat Dashmoola Taila* used *Nasya* for treatment of Migraine<sup>[16]</sup>. Most of the contents in *Brihat Dashmoola Taila* are having

*Shothahara* (anti-inflammatory), *Vedanasthapana* (analgesic), *Deepana* (appetizer), *Pachana* (digestive) and *Tridosha Shamaka Karma*. In the study of Shweta *et al.*,

*Brihat Jeevakadya Taila* was used for *Nasya* <sup>[17]</sup>. *Brimhaniya* (nourishing), *Rasayana* (rejuvenation), *Jivaniya* (anti-aging), *Dahaprashamakaaa* are the majority of drugs in *Brihat Jeevakadya Taila* (pacifying burning sensation). It pacifies *Vata-Pitta Dosha* by virtue of its *Madhura-Tikta Rasa* and *Guru-Snigdha guna*. The motility of the blood vessel wall can be regularised by *Vata* pacification action. The properties of *Pitta Shamana* can inhibit the release of inflammatory mediators such as serotonin, prostaglandins, etc. It enhances microcirculation by *Kapha* pacifying action at the *Srotasa* level, thus enabling improved tissue perfusion and nourishment. These drugs are likely to induce *Srotovishodhana* or micro-channel cleaning, thereby encouraging micro-circulatory activity, resulting in the desired *Rasayana* effect and improved nutritional status. Among *Jangama Sneha*, *Ghritha* is supreme. By virtue of its *Sanskaranuvartana* property, it attains the properties of ingredients without losing its own. *Ghritha* is effective in subsiding *Pittaja* and *Vataja* disorders; it improves *Dhatus* and is overall booster for improving *Ojas*. <sup>[18]</sup> Digestion, absorption and delivery to the target organ are made easy when any drug is processed with *Ghritha* due to its lipophilic action. *Go-Ghritha* due to its Vitamin A and Vitamin E content <sup>[19]</sup>

### Conclusion

This study was done to review the management of migraine by using *Laghu Sutashekhara Rasa* orally, *Sutashekhara Rasa*, *Brihat Jeevakadya Taila*, *Go -Ghritha* and *Brihat Dashmoola Taila Nasya*. The aforesaid Ayurvedic intervention carried out previously were effective not only in relieving the cardinal features, but also helps in relieving constipation and acidity. Ayurvedic interventions provided better result in comparison to modern intervention and placebo.

### Competing Interests disclaimer

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

### References

- Leonardi M, Steiner TJ, Scher AT, Lipton rB. The global burden of migraine: measuring disability in headache disorders with WHO's Classification of Functioning, Disability and Health (ICF). *J Headache Pain*. 2005; 6(6):429-40.
- Leonardi M, Steiner TJ, Scher AT, Lipton rB. The global burden of migraine: measuring disability in headache disorders with WHO's Classification of Functioning, Disability and Health (ICF). *J Headache Pain*. 2005; 6(6):429-40.
- Shapiro RE, Goadsby PJ. The llong drought: the dearth of public funding for headache research. *Cephalalgia*. 2007; 27(9):991-4.
- Steiner TJ, Stovner LJ, Vos T, Jensen R, Katsarava Z. Migraine is first cause of disability in under 50s: will health politicians now take notice? *J Headache Pain*. 2018; 19:17.
- Disease GBD, Injury I and Prevalence C Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017; 390:1211–1259 2017/09/19.
- Madhavakara, Madhava Nidana, Yadunandan Upadhyaya, editor. *Shiroroga Nidana* chapter 60. Varanasi: Chaukhamba Prakashana, 2010, 392.
- Shashtri Laxmipati, Yogratnakara, Shashtri Bhrahmasankar, Uttarardha, editor. Varanasi: Chaukhamba Prakashana. Ch.25/3-4, 2013, 331.
- Charaka. *Charaka Samhita. Sutra Sthana 17/22* with Vidyotini. Hindi Commentary by Kashinath Shastri and Gorakha Nath. Varansi: Chaukhambha Bharati Academy, 2011, 334p.
- Parekh Hemal. A Clinical Study on Role of Brihat Dashamoola Taila Nasya & Laghu Sutashekhara Rasa in the Management of Ardhavabhedaka w.s.r. to Migraine. Jamnagar, India: IPGT & RA, 2008.
- Shweta Mata. Clinical Evaluation of an Ayurvedic Therapy: Sutashekhara Rasa and Brihat Jeevakadya Taila Nasya in the Management of Ardhavabhedaka (Migraine). *International Journal of Ayurvedic Medicine*. 2015; 6(2):150-159p.
- Vaghela DBA. Clinical study on Ardhavabhedaka–Migraine and its management with Laghu Sutashekhara Rasa and Brihat Dashamoola Taila Nasya. Jamnagar, India: IPGT & RA, 2015.
- Shweta Mata- A clinical study on Management of Ardhavabhedaka (migraine) with Laghu Sutashekhara Rasa and Brihat Dashmoola Taila Nasya, 2018.
- Charaka. *Charaka Samhita. Siddhi Sthana 9/88* with Vidyotini. Hindi Commentary by Kashinath Shastri and Gorakha Nath. Varansi: Chaukhambha Bharati Academy, 2011, 1070.
- Charaka. *Charaka Samhita. Sutra Sthana 5/62* with Vidyotini. Hindi Commentary by Kashinath Shastri and Gorakha Nath. Varansi: Chaukhambha Bharati Academy, 2011, 123.
- Sharangdhar Acharya. *Sharangadhar Asamhita. Madhyama Khanda 9/15*. Shailja Shrivastva. Varansi: Chaukhambha Surbharati Series, 2007, 217.
- Govind Das Sen. *Bhaisajya Ratnavali, Shiroroga Prakarana. 65/94-98*. Varanasi: Chaukhambha surbharati prakashana, 2005, 1024.
- Jagdishprasad Tripathi. *Chakradutta 60/27*. 5th Edn. Varansi: Chaukhambha Sanskrita Series, 1983, 222.
- Charaka. *Charaka Samhita. Sutra Sthana 13/14* with Vidyotini. Hindi Commentary by Kashinath Shastri and Gorakha Nath. Varansi: Chaukhambha Bharati Academy, 2011, 258.
- Hari Sharma. The Effect of Ghee (Clarified Butter) on Serum Lipid Levels and Microsomal Lipid Peroxidation. *Ayu*. 2010; 31(2):134-140.