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THE EFFECT OF SPHENOPALATINE GANGLION BLOCK(SPGB) USING TRANSNASAL TOPICAL BUPIVACAINE FOR THE ACUTE TREATMENT OF CHRONIC MIGRAINE.

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ABSTRACT The neurovascular disorder migraine is one of the most common diseases worldwide. There are many medical treatment options available for chronic migraine, but these treatment options often found to have significant side effects. Sphenopalatine ganglion is a parasympathetic ganglion composed of sensory and autonomic nerves. This neural structure is located deeply in the pterygopalatine fossa posterior to the middle turbinate and maxillary sinus on each side of the face. Here we study the effect of sphenopalatine ganglion block(SPGB) using transnasal topical bupivacaine for the acute treatment of chronic migraine. **Materials and Methods-** It is a double blinded randomized controlled study. A study was conducted on 100 patients coming with acute episode of chronic migraine who were randomized in to two groups to receive 0.5% bupivacaine or saline respectively to undergo SPGB. Pre treatment NRS score was documented and post t reatment NRS assessed at 15 mins, 30 mins, 24 hours and at the end of 1 st and 6 th month and compared with the baseline NRS. **Results:** A total of 100 cases were enrolled in the study. In Bupivacaine group, the mean NRS score decreased significantly from a baseline of 6.7 to 3.8(43.3% reduction) and 3.8(43.3% reduction) at 30 mins and at the end of 6 th month respectively after repeated SPGBs. **Conclusion:** Transnasal topical sphenopalatine ganglion block is effective in acute treatment of chronic migraine.

KEYWORDS : Chronic migraine, sphenopalatine ganglion block, numeric rating scale.

INTRODUCTION

Migraine is a common primary headache disorder , causing significant disability and personal, societal, and financial burden[1]. Migraine is currently ranked by the World Health Organisation(WHO) as 19th among causes for years lived with disability[2]. According to ICHD-III beta criteria chronic migraine(CM) is defined as 15+ days/month of headache lasting >4 hours for atleast 3 months with atleast 8 days of headache[3].

Migraine treatment can be divided in to acutely acting and preventive treatment. The acutely acting treatment can be further subdivided into migraine specific treatment and analgesics, which are non specific drugs[4]. Several studies have shown that migraine patients with poor response to acute treatment are at increased risk for transformation to chronic migraine(CM), with roughly 2.5-3.5 fold greater odds of developing CM[5], so treating acute migraine attacks plays an important role.

Sphenopalatine ganglion(SPG) block has gained interest as an effective treatment modality for migraine and other headache and facial pain syndromes[6]. SPG, also known as the pterygopalatine ganglion(PPG), is a large extracranial parasympathetic ganglion with multiple neural connection including autonomic, motor, and sensory. This complex neural structure is located deeply in the pterygopalatine fossa(PPF) posterior to the middle turbinate and maxillary sinus on each side of the face.

As acute migraine attacks, as well as other primary headache disorders like cluster headache, are often associated with signs of parasympathetic activation, including lacrimation, nasal congestion, and conjunctival injection, blocking the sphenopalatine ganglion, which is the major parasympathetic outflow to the cranial and facial structures, is a reasonable target to help relief pain and autonomic features seen in this disorder.

From an anatomical and physiological perspective, Sphenopalatine ganglion block is considered to be a comfortable, efficient, and safe method for managing craniofacial pains[7]. There are various approaches described for this procedure of which transnasal approach using local anaesthetic agent is a less invasive, easy and safe method of pain relief[8].

So, the present study was conducted in order to determine if repetitive sphenopalatine ganglion(SPG) blocks with 0.5% bupivacaine delivered using sterile culture swabs are superior in reducing pain associated with chronic migraine(CM) compared with saline.

Objectives

To study the effect of sphenopalatine ganglion block using transnasal topical bupivacaine for the acute management of chronic migraine.

Review Of Literature

Background

Headache is an extremely common symptom in our society. Headache is responsible for large amount of absenteeism from work and school and for a large expenditure on medications and investigations[9]. Probably more important from a public health aspect are the severe risks run by thousands of patients who are heavily self medicated to relieve or prevent headache.

Epidemiology

Onset of migraine is from childhood onwards but most commonly in the 20s and 30s and relatively infrequently after the age of 40 years. The prevalence increases from the first to fourth decades and thereafter declines[10]. Overall, migraine has a variable prevalence worldwide. Probably everywhere, significantly more women are affected than men, in a ratio of 2-3:1[11].

Pathophysiology

Exact pathogenetic mechanism that causes migraine remains allusive. Migraine is now thought to be sensitive brain disorder which manifests as episodic bursts of headache. The causes of increased neuronal excitability underlying the sensitive brain are probably multifactorial and may be located at different levels of neural axis from cortex to the nerves supplying the blood vessels in the trigeminal and cervical area[12].

Excitability of neurons that in supposed to underlay the sensitive brain of migraine is partly genetically determined and this is what makes the brain susceptible to attacks. Factors that tend to increase the neuronal excitability prevent or terminate the attacks.

Neuronal Hyperexcitability in Migraine:

A study by Thomas et al demonstrated CO2 reactivity with transcranial doppler[13]. Sakai and Meyer had shown cerebral hyperperfusion and abnormal cerebrovascular reactivity during migraine suggesting increased neuronal activity[14]. There are EEG studies that have shown

enhanced photic stimulation response[15].

Transcranial magnetic stimulation is a technique that provides a new opportunity to investigate the relationship between migraine and neuronal hyperexcitability more directly and noninvasively.

The sensory sensitivity that is characteristic of migraine is probably due to dysfunction of monoaminergic sensory control systems located In the brainstem and thalamus.

Data also supports a role for dopamine in the pathophysiology of migraine. Most migraine symptoms can be induced by dopaminergic stimulation.

Factors Responsible For Hyperexcitability Of Brain

Evidence of Mitochondrial Dysfunction:

Migraine like attacks are often a part of the symptomatology of some mitochondrial disorders like MELAS syndrome(mitochondrial myopathy, encephalopathy, lactic acidosis and stroke like syndrome). It is well known that in mitochondrial disorders the cellular energy metabolism is disordered[16].

Role of Magnesium in Hyperexcitability of Neurons:

Magnesium is one of the many factors that influences energy metabolism and also mitochondrial function. There is increasing evidence now which suggests that there is a deficiency of magnesium in the brains of migraine patients[17].

Role of Nitric Oxide in Hyperexcitability:

The non specific headache is caused by activation of cGMP while the delayed migraine may be due to nitroglycerin acting as the nitric oxide donor which triggers the typical headache[18]. Lassen et al[19] showed 1-methylarginine hydrochloride a non specific inhibitor of nitric oxide synthase gave relief in 10 of 15 patients with migraine.

Principles of Acute Treatment

Migraine may not always begin as pain, but instead may present as a prodrome of mood change, fatigue, muscle tension, yawning, cognitive dysfunction, or other vague symptoms[20].

The patient should be treated early in the attack, use an adequate dose and formulation of a medication appropriate to the circumstances, maintain hydration, and seek rest if necessary.

Nonspecific Acute Treatment

Nonsteroidal Anti-inflammatory Drugs/Acetaminophen:

Nonsteroidal anti-inflammatory drugs(NSAIDs), such as acetylsalicylic acid(ASA), ibuprofen, naproxen sodium, indomethacin, diclofenac, and ketoprofen, have long been used alone or in combination with other agents for the acute treatment of migraine.

Dopamine

D2 receptor antagonists, used alone or in combination, may treat headache pain in addition to migraine-associated nausea[21,22].

Prochlorperazine, available in 5-mg or 10-mg tablets and 25-mg suppositories, may be effective in acute migraine, alone or in combination with triptans or NSAIDs.

Corticosteroids

One small study suggests benefit from a single oral dose of dexamethasone to prevent headache recurrence after initial treatment with a triptan and NSAID[23].

Specific Acute Treatment

Triptans:

Triptans are selective serotonin 5-hydroxytriptamine 1B and 1D(5-HT1B, 5-HT1D) receptor agonists[24] with three postulated mechanisms of action: intracranial vessel vasoconstriction(5-HT1B), peripheral neuronal inhibition(5HT1D), and presynaptic dorsal horn stimulation(5HT1D) producing second-order brainstem neuronal inhibition.

Ergots:

Clinicians continue to prescribe ergot alkaloids in the acute treatment of migraine and some patients find them more efficacious than triptans. Ergots are less specific than triptans in their serotonin receptor agonism and interact with multiple other receptors, possibly explaining their more robust side-effect profile[25].

Sphenopalatine Ganglion

The sphenopalatine ganglion(SPG) is the largest of the peripheral parasympathetic ganglia and is located in the pterygopalatine fossa. Recent research is defining the sphenopalatine ganglion's key role in the pathophysiology of different headache syndromes including cluster headaches, migraines, and trigeminal autonomic cephalalgias (TACs)[26,27,28]. The effectiveness of electrical stimulation of the SPG for acute treatment of intractable migraine and cluster headaches has recently been demonstrated[29,30].

Anatomy And Physiology Of Sphenopalatine Ganglion(SPG):

The SPG has sensory and autonomic components. The autonomic components are particularly relevant to its effects on cerebrovascular physiology and consists of both parasympathetic and sympathetic components.

Transnasal Approaches For Sphenopalatine Ganglion Block:

Sluder[31] first proposed transnasal blockade of the SPG using topical cocaine applied transnasally. Thus, topical application of anaesthetic solutions such as lidocaine applied to the posterior wall of the nasopharynx in the region of the middle turbinate can diffuse across the mucosa to alter activity within the SPG.

Procedure

The patient is placed in supine position with the neck extended. The posterior nasal pharynx is anaesthetised and lubricated by asking the patient to inhale a small amount of 2% viscous lidocaine instilled in to the nares. For topical block of the sphenopalatine ganglion, a sterile 10 cm cotton tipped applicator dipped in 4% lidocaine and slowly advanced along the superior border of the middle turbinate until it reaches the posterior wall of the nasopharynx. The applicator is usually left in place for approximately 20-30 min to diffuse across the mucosa and take effect.

Though SPG blockade via the transnasal approach is reported effective in some studies in migraine and cluster headache the procedure does have potential adverse events(AEs) such as epistaxis, rare central nervous system(CNS) infections, and the certainity of getting an anaesthetic agent to SPG is unpredictable[32].

MATERIALS AND METHODS

Study Setting:

Department of Otorhinolaryngology, Navodaya Medical College Hospital and Research Centre, Raichur.

Study Population:

Study was conducted on 100 patients coming with acute episode of chronic migraine to the Out Patient Department of Otorhino-laryngology. Navodaya Medical College Hospital and Research Centre, Raichur.

Study Design: double blinded randomized controlled study.

Sampling Technique:

Study was conducted from October 2019 to June 2021 involving 100 patients who were randomized in to two groups to receive 0.5% bupivacaine or saline respectively.

Inclusion Criteria:

Acute episode of chronic migraine(according to the criteria proposed by the headache classification committee of the international headache society) for atleast 3 months prior to enrollment.

- Onset of migraine before age of 50 years.
- Able to differentiate migraine from any other headache they may experience(eg.tension type headache).
- Is not currently taking any medication.

Exclusion Criteria:

- Nasal septal deformity such as cleft palate, choanal atresia, atrophic rhinitis, rhinitis medicamentosa.
- Septal perforation.
- Recent nasal/sinus surgery.
- Bleeding disorders like von Willebrand disease or hemophilia.
- Severe respiratory disorder.
- Allergy to bupivacaine.
- Had nasal congestion present more than 10 days with fever(temperature>100.4^{0}F).
- Known to be pregnant, or breast feeding.

Methods of Data Collection:
Patients who satisfied the above mentioned criteria for selection were taken as subjects for the study, after taking an informed and written consent.

Details were subjected to a general physical examination and through a local examination of ear, nose and throat. Laboratory investigations like CBC, bleeding time, clotting time was done.

Bupivacaine test dose was given prior to procedure for those subjects who were randomized under bupivacaine as a study drug.

Procedure

- As our study is a double blinded randomized controlled study, designator assigns the drug prior to procedure which was blinded to both investigator(treatment provider) and subjects.
- As per randomization chart, designator hands over the drug to the treatment provider.
- Before the procedure, Pain was assessed using numeric rating scale(NRS), where 0 is no pain and 10 is worst pain imaginable.

Description of the Procedure:

- Nose was inspected for any obstruction, and xylometazoline 0.05% nasal drops(one drop in each nostril) were used to help open nasal passages.
- Patient was made to lie in the supine position with head extension, A small amount of 2% lidocaine jelly was instilled in each nostril for patients comfort.
- As per randomization which was done before, each patient received a trans nasal SPG block either with 2cc of 0.5% bupivacaine or 2cc of saline in each nostril by using sterile culture swab.
- By using thudicum's nasal speculum, swab stick is inserted through the anterior nasal passage parallel to nasal septum and above the middle turbinate until the resistance is met. Procedure was repeated on the other side.
- Patients were allowed to rest in supine position for 5-10 minutes and swab sticks were removed carefully without injuring the nasal mucosa.
- NRS was recorded at 15 minutes, 30 minutes, and 24 hours after the procedure.
- Procedure was repeated 2 times per week for 6 weeks and re-evaluated with NRS at 1st month and 6th month and compared with the baseline.
- Side effects experienced by all subjects during the active treatment phase was noted.

Statistical Analysis
Results are presented as Mean+_ SD and range values for continuous data and frequencies as numbers and percentages. Intergroup comparisons were done by unpaired t test and Paired t test for intra group comparisons. Categorical data was analysed by Chi-square test.

P value of 0.05 or less was considered for statistical significance.

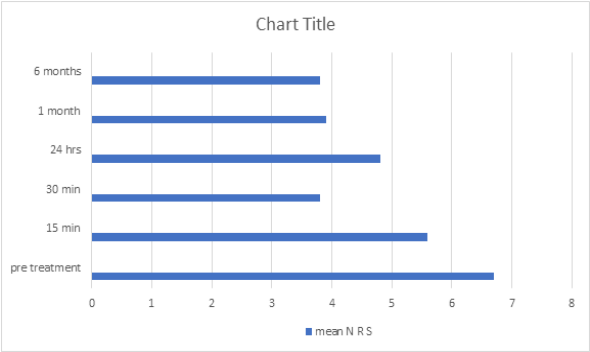
SPSS(Version 18) software was used for data analysis.

OBSERVATIONS AND RESULTS
A total of 100 cases were chosen with chronic migraine satisfying inclusion and exclusion criteria attending the out-patient department at Navodaya Medical College and Hospital, patients who were randomized in to two groups to receive 0.5% bupivacaine or saline SPGB respectively.

Table 1. Intragroup Comparisons Of Changes In Nrs Scores From Pretreatment To Post Treatment With Bupivacaine 0.5%.

Time of assessment		BUPIVACAINE 0.5%				
		Mean ± SD	Reduction from Pre-Treatment	% Reduction	t value	P value
Pre-treatment		6.7±1.3	-	-	-	-
Post treatment	15 min	5.6±1.2	1.1	16.4%	16.80	0.00**
	30 min	3.8±1.2	2.9	43.3%	27.88	0.00**
	24 hours	4.8±1.2	1.9	28.3%	15.09	0.00**
	1 month	3.9±1.3	2.8	41.8%	20.61	0.00**
	6 months	3.8±1.2	2.9	43.3%	21.16	0.00**

Paired t test **P<0.001, HS



Graph 1

Mean pretreatment NRS(pain score) of patients who were randomized under bupivacaine group was 6.7±1.3(Mean+-SD).

Post bupivacaine sphenopalatine nasal block, NRS was assessed and it was found that there was 16.4%(5.6±1.2) reduction in NRS at 15 min post procedure. Significantly about 43.3%(3.8±1.2) reduction in NRS score was noted at 30 mins post procedure. About 28.3%(4.8±1.2) reduction in NRS score was found at the end of 24 hours.

Patients were followed up twice in a week for 6 weeks for subsequent SPGB blocks NRS evaluation was done at the end of 1st and 6th month.

At the end of 1st month, there was 41.8%(3.9±1.3) reduction in NRS score and at the end of 6th month there was significant reduction in NRS score noted that is about 43.3%(3.8±1.2). Patients who underwent SPGB with bupivacaine 0.5% had a significant(**P<0.001, HS) reduction in pain score at each visits.

Table 2 Intragroup Comparisons Of Changes In Nrs Scores From Pre-treatment To Post Treatment With Saline

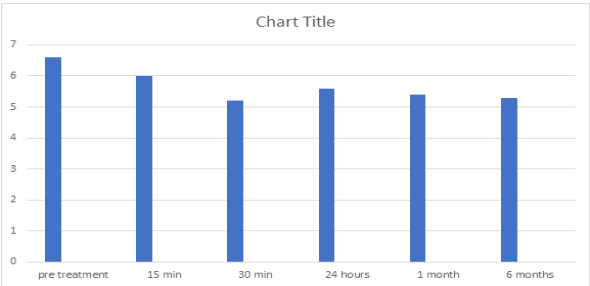
Time of assessment		BUPIVACAINE 0.5%				
		Mean ± SD	Reduction from Pre-Treatment	% Reduction	t value	P value
Pre-treatment		6.6±1.1	-	-	-	-
Post treatment	15 min	6.0±1.1	0.6	9.1%	7.94	0.00**
	30 min	5.2±1.1	1.4	21.2%	16.2	0.00**
	24 hours	5.6±0.9	1.0	15.2%	8.98	0.00**
	1 month	5.4±1.0	1.2	18.2%	12.04	0.00**
	6 months	5.3±1.0	1.3	19.7%	12.24	0.00**

Mean pretreatment NRS(pain score) of patients who were randomized under saline group was 6.6±1.1(Mean+-SD).

Post saline sphenopalatine nasal block, NRS was assessed and it was found that there was 9.1%(6.0±1.1) reduction in NRS at 15 min post procedure. Significantly about 21.2%(5.2±1.1) reduction in NRS score was noted at 30 mins post procedure. About 15.2%(5.6±0.9) reduction in NRS score was found at the end of 24 hours.

Patients were followed up twice in a week for 6 weeks for subsequent SPG blocks. NRS evaluation was done at the end of 1st and 6th month.

At the end of 1 st month there was 18.2%(5.4±1.0) reduction in NRS score and at the end of 6 th month there was significant reduction in NRS score noted that is about 19.7%(5.3±1.0).
Patients who underwent SPGB with saline too had a significant(**P < 0.001, HS) reduction in pain score at each visit.



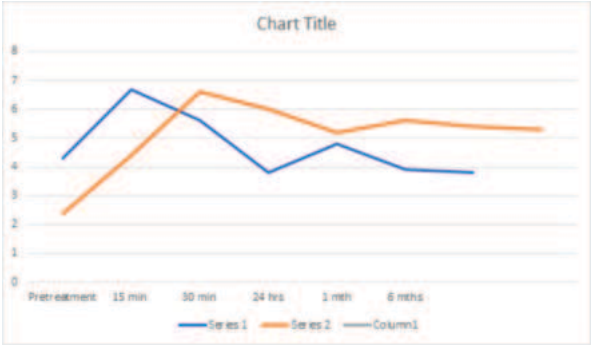
Graph 2

Table 3 Comparison Of Nrs Scores Between Two Treatments At Different Times Of Assessment.

Time of assessment		BUPIVACAINE 0.5%		SALINE		BUP V/S SALINE	
		Mean	Range	Mean	Range	t	P
Pre-treatment		6.7±1.3	4-9	6.6±1.1	4-8	0.58	0.65, NS
Post treatment	15 min	5.6±1.2	3-8	6.0±1.1	4-8	1.58	0.16, NS
	30 min	3.8±1.2	2-7	5.2±1.1	3-7	6.10	0.00**
	24 hours	4.8±1.2	2-7	5.6±0.9	4-8	3.94	0.00**
	1 month	3.9±1.3	2-7	5.4±1.0	3-7	6.30	0.00**
	6 months	3.8±1.2	2-6	5.3±1.0	3-7	7.01	0.00**

Unpaired t test **P < O.OO1, HS P > 0.05, Not Significant.

Upon comparing the NRS scores between two treatments at different times of assessment, no significance was seen in pretreatment NRS score and 15 min post procedure NRS score, but there is significant difference in NRS score between groups at 30 min, 24 hrs, end of 1 st and 6 th month.



Graph 3

Comparison Of Nrs Scores Between Two Treatments At Different Times Of Assessment.

DISCUSSION

A total of 100 cases were chosen with chronic migraine satisfying inclusion and exclusion criteria attending the out patient department at Navodaya Medical Hospital. After randomization, patients were divided equally in to two groups to receive 0.5% bupivacaine and saline SPGB respectively.

In our study, in bupivacaine group who underwent Sphenopalatine ganglion block, the mean NRS score decreased significantly from a baseline of 6.7 to 5.6(16.4% reduction), 3.8(43.3% reduction), 4.8(28.3% reduction), 3.9(41.8% reduction) and 3.8(43.3% reduction) at 15 mins, 30 mins, 24 hours, end of 1 st month and 6 th month respectively.

In saline group who underwent sphenopalatine nasal block, the mean NRS score decreased significantly from a baseline of 6.6 to 6.0(9.1% reduction), 5.2(21.2% reduction), 5.6(15.2% reduction), 5.4(18.2% reduction) and 5.3(19.7% reduction) at 15 mins, 30 mins, 24 hours, end of 1 st month and 6 th month respectively.

In a study conducted by Lee Kudrow et al, in 12 successfully treated patients, post treatment pain intensity scores of 0 to 1 were achieved within 2 minutes by 5 patients, 5 minutes by 3 patients, 15 minutes by 3 patients; and 30 minutes by 1 patient[33].

In the study conducted by Maizel and Geiger et al, there was significant reduction in headache severity at 15 minutes compared to placebo. In this controlled trial, headache was relieved within 15 minutes in 34(35.8%) of 95 subjects treated with 4% intranasal lidocaine compared with 8(7.4%) of 108 subjects receiving placebo[34].

CONCLUSION

At the end of the study, we concluded that sphenopalatine ganglion block using bupivacaine is a safe, comfortable, easy and efficient method to manage acute episodes of chronic migraine.

Patients who underwent SPGB using bupivacaine showed more percentage reduction in acute pain(NRS) compared to saline group and we also concluded that frequent repeated sphenopalatine ganglion block has significant effect in reducing NRS score which was noted at the end of 6 months of follow up.

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