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Electromotive Administration of Disprin for Clinical Utility of Transdermal Iontophoresis in Acute Migraineurs – A Case Report

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ABSTRACT

Background: Migraine is a recurrent headache disorder with varying symptoms like nausea, vomiting and hemi cranial pain. It is considered to be one of the most disabling disorders, which impair ability of functioning and also affects quality of life. In most of the cases it was very commonly seen that there are gastric problems associated with medications and other severe consequences after ingestion among migraineurs.

Epidemiology: Migraine headache is one of the most common types of brain disorders and commonest subdivision of primary type of headache (asper classification of headache disorder, 2004). In India, the 1year prevalence of migraine (n = 1,488)in the targeted study population was 63.9 %, with female predominance(73% in females in comparison to 54.4 % in males; OR = 2.3[1.9-2.7]) and urban predominance(71.2 % urban versus 57.3 % rural; OR = 1.8{1.6-2.1}). It is affecting 15% of the population duringtheir most productive time of their lives. Mostly affected population is between the age of 22to 55 years. It sometimes starts in childhood and mostly around puberty. It affects femalesmore than males, the ratio of female: male is 3:1.

Clinical features: Symptoms of migraine attack develops with a trigger like stress, hunger, weather change etc. and it develops gradually with varying autonomic symptoms like nausea, vomiting, hemicranial pain etc. with some cognitive symptoms and sensory symptoms.

Methodology: The patient was a female of age 37. She was suffering with migraine attack since morning and was diagnosed as migraine by a Neuro Physician. Then she came to Physiotherapy OPD department for treatment. She was assessed on the MIDAS migraine scale in the physiotherapy department; the score was 21 on MIDAS scale.

Treatment and Result: Iontophoresis technique is a transdermal and non-invasive method for drug transfer, which works with the use of low electrical current to move ionized drug particles across the skin, then reach up tothe underlying tissue and blood vessels. The solution was prepared with oneDisprin pill contains 300 mg of 2-hydroxybenzoic acid.

Once disprin pill dissolved in 3000 milliliter (3 Liters) of water provides 100% answer. If we wish 5% of desired solution then dissolve seventy-five mg in 1500 milliliter (1.5 Liters) of water.

When the electric current is applied to the aspirin with the positive electrode (i.e. anode), it pushes the disprinthrough the skin into the deeper structures like subcutaneous tissue and it is absorbed from the cervical bloodvessel. Patient was then provided the iontophoresis treatment by transdermal patch techniquewith 5% aspirin solution for 20 minutes.

Then patient was reassessed on MIDAS scale just after the treatment; the score was 10.

Conclusion: Iontophoretic method of treatment could be proven best way to be given disprin without having gastric side effects.

Keywords: Transdermal Drug Delivery, Iontophoresis, Disprin, Aspirin, Basilar Artery.

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INTRODUCTION

Globally Migraine headache is a most common chronic neurologicalbrain condition. It is a Global burdened disease. In one study, in 2015 it was ranked 3rdmost common cause of disability around the world in both males and females under the age of 50 years.1 There are various approaches for drug delivery in migraine patients such as Oral, Intranasal, Transdermal, Injections and Infusions. In most cases, orally drug ingestion is very common and convenient route of drug administration as it is cost-effective, portable and easy to use. However, there are some limitations with oral drug ingestion, such as incomplete absorption due to the unpredictability of multiple factors of gastrointestinal(GI) tract.Issues related to oral administration of NSAIDs are allergies occur due to NSAIDs(like Ibuprofen. Disprin), blood clotting problems, gout, menorrhagia , liver or kidney disease, stomach ulcers or gastrointestinal bleeding or bleeding tendencyin other organ system, nausea, dizziness and vomiting are also associated in migraineurs with a migraine episode. In previous studies Thirty-one percent of patients had experienced nausea and forty two percent of those who previously experienced vomiting stated that these symptoms interfered with ingestion of orally migraine medications.2Transdermal Drug Delivery or Ingestion (TDD) is now a day new promising way for drug application and transmission that has major influence over some of the most common route of drug administration and absorption. Transdermal Drug Delivery consists of noninvasive delivery of medications like aspirin through the dermis and when applied over the dermis can deliver the drug at a fixed pre-determined rate across to achieve some of either a local or systemic effect.Iontophoretic transdermal Medicine or a drug delivery system uses a electric current to push charged molecules of medicine into the dermis under an electrode of same polarity (anode or cathode) and offers an better option to facilitate the delivery of macromolecules or hydrophilic molecules and it improves patient's compliance.3We present a case referred to our physiotherapy department treated successfully with the iontophoretic transdermal drug delivery system using aspirin as the delivered drug.

Case Description:
A 37-year-old male diagnosed as a case of migraine 3 months back by a neurologist of our institute was referred to the department of physiotherapy. Patient had been receiving oral NSAIDs and Beta Blockers for the last 3 months. With oral medications patient had a mild improvement in his pain and worsening of symptoms was not seen. Patient also avoided the aggravating factors for his headache since last 3 months. On the first day of referral to the physiotherapist, patient had been experiencing severe headache since early morning and despite taking his medications pain was persisting. On arrival in the physiotherapydepartment patient was having hemi-cranial pain along with cervical pain and tenderness on same side. Pain was throbbing and continuous in nature. On Numeric Pain Rating Scale (NPRS) his pain was scored 8/10. He had a score of 21 on the MIDAS migraine scale.

Intervention:
After assessing the patient, conventional physiotherapy was given for 20 minutes. Conventional physiotherapy included cranial base release technique, neck flexion exercises and neck isometrics.

Patient had little relief with the conventional physiotherapy NPRS (7/10). Patient was thenexplained about iontophoretic transdermal delivery procedure and a written consent was obtained. A 5% Disprin solution was madeby adding 75mg Disprin in 1500 ml of water. Site of application of electrodes were cleaned with betadine solutionand then sterile gauge. We used Eletromed Combo Therapy (Vectrostim-100 / Technomed Electronics) for the procedure.

Anodic electrode wrapped in a lint cloth was dipped in 5% Disprin Solution and was applied over Sub-Occipital Triangle. Cathodic electrode was applied over right forearm.

Metallic electrodes measuring 2 x 3 cms. were used for the both the sides. Plain DC current at the rate of 0.5 mA/cm2 was applied for 20 minutes (Total 40 mA 0. After the completion of procedure patient was reassessed and pain was found to be reduced significantly NPRS 2/10 and MIDAS 10.

Chart: 1

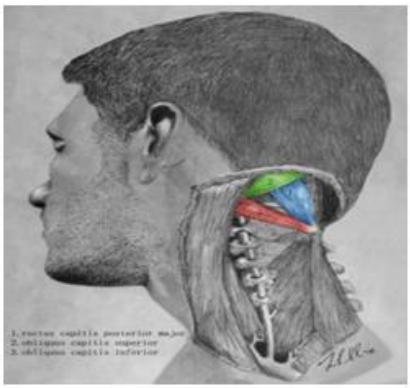
	Pre	**After Conventional Physiotherapy**	**After Iontophoresis**
NRPS	8/10	7/10	2/10
MIDAS	21	20	10

DISCUSSION

In India migraine is one of the leading causes of primary headache disorder. On an average, in India, the 1year prevalence of migraine (n = 1,488)in the targeted population study in 2015, it was 63.9%, with female predominance (73.0% in females as compared to 54.4% in males; OR = 2.3 {1.9-2.7}) and urban predominance (71.2% urban versus 57.3% rural; OR = 1.8 {1.6-2.1}).4Aspirin, acetaminophen and NSAIDs are the most commonly used drugs for the treatment of any headache and migraine, and migraineur patients use them as over-the-counter drugs.

Migraine was always known as vasospastic disorder, which initiates with vasoconstriction in cranial vasculature.5 After the early vasoconstriction stage, blood vessels in meninges dilates which activates trigeminal sensory nerves that surrounds the meninges and causes pain in meninges. This further activation of trigeminal nerve causes vasoactive neuropeptides release. Following this event, it contributes to the dilation that causes neurogenic inflammation and pain sensitive cranial structures and worsens the headache.

The vertebral artery (right and left) arises from the posterior-superior part of the central subclavian arterieson each side of the body. Then it enters deeply into the transverse process from C6 (in 40% cases from C7)6 to C2. Then it proceeds superiorly in each transeverse foramen of cervical vertebrae, then it proceeds across the posterior arch of C1(also called Atlas)and goes through the Suboccipital angle before it enters in the foramen magnum.7



Iontophoresis device entails propelling a charged substance, usually medication or else bioactive agents, through a membrane by repulsive electromotive force. Iontophoresis technique is well classified for transdermal applications, where as it enhances drug delivery by a combination of electro-repulsion and electro-osmosis, dominant force in mass ionic transport.8, 9

This unique delivery method of transferring medications has not been used, but currently being used with patch system for the treatment of a number of different conditions with some of the same concept. Some of them are shown in table.10

Table: Examples of skin patches(not for iontophoretic device) and patch delivery system for transferring medications

S. No.	Diseases or other medical conditions	Pharmacological Combinations
1.	Pain due to any reason	Non-Steroidal Anti-Inflammatory Drug(NSAID)
2.	Alzheimers disease	Rivastigmine Medicine
3.	Anaesthesia (local or topical application, especially for paediatricuse)	Lidocaine + Adrenaline(Epinephrine) Nitroglycerin
4.	Angina attack	Insulin
5.	Diabetes mellitus(DM)	Methylphenidate
6.	Attention Deficit Hyperactivity Disorder(ADHD)	Clonidine
7.	Hypertension(HTN)	Dexamethasone
8.	Inflammation in conditions like bursitis, plantar fasciitis and hyperhidrosis etc.	Fentanyl
9.	Treatment for neuropathic pain due to cancer and some other severe and chronic pain	Acetylcholine
10.	Vasodilator	

Medications required to treat migraine,are associated with complications like severe disability and neuroautonomic disorders like acidity. Visual and other types of aura, gastric stasis which causes poor absorption from thestomach tissue lining, dizziness, nausea, vomiting, vertigo that might worsens with movement (kinetophobia), phonophobia, osmophobia, photophobia and balancing difficulty.11 Low bioavailability due to gastroparesis might be cause for treatment failure. The incidence of gastric stasis or decreased gastrointestinal movement during migraine attack causes decreased absorption rate of aspirin and Paracetamol and other drugs.

One of the most common problematic and increasing chief complaint associated with migraine is that the disabling and deteriorating effect of medication intake has on its treatment, which is a major disadvantageand obvious discomfort it causes to the migraine sufferer. Patients who feltnauseatic in previous treatment may either delay or even avoid oral treatment or altogether. However, these abovesaid medications are most often associated with side effects such as sedation, heaviness, akathisia and some tomes dystonic reactions.

CONCLUSION

Iontophoretic transdermal drug delivery is an effective way of drug delivery. Use of this method of transfusing drugin migraine patients will help in avoiding adverse effect caused by systemic administration of drug.

Further research is required to determine the optimal current dosage, application procedure and number of sessions that will increase the efficiency of this procedure. Studies with large number of participants are needed to assess effects, adverse reactions and compliance of this method. Still, this presents a new system of drug delivery for migraineurs having contraindications or adverse effects with oral or injectable drugs.

Limitation of the study

This study limits ample of patient data. It needs further study in large no. of population. It also requires seeing the effect of more sittings as well as following up of the patient.

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