

Therapeutic opportunities for headaches and migraines in pediatric populations: A Review

Abstract:

Headaches, migraine-like episodes, and other associated conditions which are increasingly becoming the most frequent occurrence and a threat to the pediatric population in today's world. It has become the most sought-after therapeutic opportunity in the clinical setting in a way which can help to treat, diagnose and minimize its ill effects or side effects in today's world which has witnessed all severe form of diseases and hopefully will witness more severe forms because of the everlasting unhealthy lifestyle and prevalent hypertension which can be maternal or paternal and can affect the new born as well as all the pediatric age groups in today's world. Severe forms of Headaches in children or in pediatric age groups can be a massive challenge for the clinician, to identify, diagnose as well as to provide effective treatment which can be curable in most of the cases but can be fatal too. In pediatric populations, headaches or migraine can be the result of underlying conditions , pathologies , or effects of maternal and paternal habits or lifestyle that need more attention than the symptom itself. The treatment spectrum ranges from pharmacological interventions to more unconventional options like acupuncture and alternative medicine. All these options are worth considering, as several studies show high efficacy and success rates with each of these conditions and etiology discussed above .In this review, the authors aim to discuss each of these different therapeutic options and weigh out their pros and cons which can help in better and effective treatment to control or eliminate this disease .

Keywords- 1. Migraine like-episodes, Prevalent Hypertension ,acupuncture, maternal , paternal , Pharmacological interventions, Therapeutic, Spectrum .

Background

Headaches can broadly be classified into primary and secondary headaches. Primary headaches, like migraine, tension type headache, and cluster headache have no such underlying pathological causes but are still considered very severe in today's clinical setting. Secondary headaches have a deeper neuropathological or systemic cause in pediatric population. Secondary headaches and it's causes pervades several medical disciplines and the underlying pathologies can vary greatly from one person to another. Causes can be classified as traumatic, inflammatory, cancerous and tumorous or those due to a rise in intracranial pressure are also important causes . Headaches are generally a part of a greater medical condition, where the condition is greater than the sum of its parts. From a bird's eye view, the incidences of primary headaches far outnumber secondary headaches in the pediatric setting in today's world . [1]

Headaches greatly affect a child's ability to carry out normal day to day activities with full potential and enthusiasm. It can exacerbate many psychological conditions like anxiety, depression, and may cause increased instances of absence from school, erratic social behavior and mental stability . Identifying and diagnosing the presence of psychosocial conditions in patients of headache can increase the likelihood of complete and effective management of the

condition and can control its fatal progress in the patient . In children and adolescents, the presence of aforementioned conditions also increases the likelihood of suicidal tendencies and other anti-social actions. Thus, it makes the management of such migraine cases a matter of public health concern and thus its importance increases to a greater extent and should be considered with much priority and should be given significant attention too.[2]

Scope of Treatment

Treatment for headaches in pediatric populations in today's clinical settings is hotly debated and highly variable from one clinician to another in general practice. Several established pharmacological interventions work wonders in almost all patient demographics around the world . There has also been a constant generation of new research regarding better and more targeted pharmacological therapies to cure and prevent this disease . These include, but are not limited to, intravenous Sodium Valproate [3] administration and intravenous dihydroergotamine [4].

However, there is also sufficient body of evidences pointing towards associated side-effects and adverse reactions that accompany these pharmacological interventions in today's setting. This has lead a new generation of practitioners to consider alternative therapy options which are highly beneficial and effective such as described below-

1. Acupuncture,
2. Behavioral management,
3. Stimulation therapy,
4. Physical therapy,
5. Transcutaneous Electrical Nerve Stimulation (TENS),
6. Transcranial Magnetic Stimulation (TMS),
7. Osteopathic manipulations,
8. Placebo therapies, and
9. Psychological counselling.

In the text that follows, we will discuss some important straight-forward pharmacological and some best alternative medical interventions to be worked upon for the betterment of the pediatric group.

Intravenous Sodium Valproate

In the treatment of Chronic Daily Headache and migraine in children, it is critical and important to have a highly effective drug which is tolerable and also has a great safety profile in terms of action, absorption and elimination. Sodium Valproate can be utilized as a single substance for the effective management of episodes of migraine or severe headache for an extended length of time . According to the findings of migraine-like headaches clinical trials and prolonged extension trials, Sodium Valproate meets this standard of treatment in today's clinical setting. The mechanism through which Sodium Valproate alleviates migraine is unknown . Many processes in the migraine cascade may be influenced by Sodium Valproate and can cause beneficial and desired effects and outcomes in the pediatric population. [5]

In a recent study into the efficacy of said drug and administration method the drug , out of the total sample size, "83% were discharge. Mean hospital admission duration before was 395

minutes, falling to 120 minutes after administration of the drug . Pain score reduction jumped from 17% before administration to 40% after the use of the drug. [3]

In the early study, The Sodium Valproate and placebo groups of patients with Chronic Migraine were contrasted. At the conclusion of the first 30 days, there were remarkable differences in certain metrics between the Sodium Valproate and placebo groups. Upon the conclusion of the 3rd month, essential parameters were decreased, and so were other migraine markers. [5]

However, in Chronic Tension Type Headache patients, Sodium Valproate therapy is only beneficial on the early parameters with less side effects . Other metrics showed no significant decreases. In an open prospective trial evaluating the preventive effectiveness of Sodium Valproate in 56 patients, including 35 migraineurs, 7 chronic tension type headache patients, and 14 patients with mixed headaches, 60% of participants improved by 3/4ths or more in the frequency of episode days while using Sodium Valproate with the prescribed dose. [5]

Thus, Sodium Valproate infusion appears to be safe and effective in pediatric populations suffering from all forms of severe headaches and migraines. There are also some non- specific treatment for pediatric population in today's clinical setting ketorolac , Ibuprofen, Naproxen are often used to treat migraine by clinicians . Some common contraindications shown by the above drugs are upper GI diseases , renal system becomes impaired and with some bleeding disorders.

Transcranial Magnetic Stimulation (TMS)

TMS (transcranial magnetic stimulation) is a very strong force field of electromagnetism produced by a current passing via a coil wound over the head or scalp. Single-pulse transcranial magnetic stimulation, pair-pulse transcranial magnetic stimulation, and repetitive transcranial magnetic stimulation are all best examples of transcranial magnetic stimulation (TMS). TMS (Transcranial magnetic stimulation) can be used to monitor neural conduction and assist or stop the electrical impulses of the cerebral cortex in neurophysiology which itself is a very dynamic and an important concept. TMS has shown enormous amount of growth in the past 8 years as FDA has approved several new devices for the treatment of severe migraine in the pediatric population.

TMS is non-invasive treatment that can excite (or decrease) the excitability of the brain in particular the cortex. Due to the lack of proper Randomized Controlled Trials, the European Headache Federation put out a statement in 2013 stating that at this time, it isn't evidence-based or advisable to use a noninvasive therapy in chronic headaches, and that a neuro-stimulator should be thought about only after all other drugs and behavioral interventions as advised by global guidelines have not been successful , drug overuse episode is excluded and with less side effects. Because there are few medicines that can help patients with migraines improve their quality of life and well being, Transcranial Magnetic Stimulation is a potential therapy that can either stimulate or block the electrical impulses generated by the cortex. [6]

We only include Randomized Controlled Trials so that we can enhance the dependability of our analysis and trail . Despite the fact that a meta-analysis of Randomized Controlled Trials can offer a more accurate conclusion and better results with detailed data , the fact that just 5 Randomized Controlled Trials were involved in the meta-analysis restricted us from achieving a more reliable result owing to a lack of studies on the subject . Subjects were not classified by intensity of infectious ailment, gender, age, or other factors in any of the studies included in the

study. As a result, the effectiveness and action of Transcranial Magnetic Stimulation should be considered with all priority. [6]

Based on the research reviewed, a meta-analysis concludes that Transcranial Magnetic Stimulation is beneficial for migraine-like episodes in pediatric population. According to the research in the publication, employing a 8-shaped loop around the levo-motor-cortex with increased frequency may be helpful for stimulation parameters. The effectiveness of TMS for migraine-like episodes should, however, be evaluated in additional RCTs in the later stages due to constraints. [6]

We found no statistically significant difference in impact between the active Transcranial magnetic stimulation group and the sham Transcranial magnetic stimulation group when evaluating the effect of Transcranial magnetic stimulation on chronic migraine or headache. In light of this, we propose the following hypothesis: chronic migraine is a persistent pathogenic process with a much higher pain threshold. Transcranial magnetic stimulation has the power to alter the excitability of the cortex, but it takes time to complete its process. [6]

Psychotherapy and Counselling

Psychological treatments are seen to be more effective when combined with the right pharmacological therapies. These therapies are highly effective in reducing the disability in pediatric patients suffering from mixed chronic pain like conditions and for children with headaches at follow-up whenever needed.

When cognitive behavioral therapy was compared to a waiting list control, the findings were inconsistent and not of any value, with some studies suggesting that cognitive behavioral therapy was more beneficial on some outcomes but not others. The findings of this research give some evidence for cognitive behavioral therapy above and beyond typical therapeutic variables for cognitive behavioral therapy with relaxation compared to relaxation alone. Cognitive behavioral therapy combined with relaxation was shown to be more helpful than antidepressants alone. However, unfavorable side effects of antidepressant medicine used may have muddled outcomes, implying that adverse side effects for some people may outweigh any potential advantages for others. [7]

Relaxation training (RT), cognitive behavioral therapy (CBT), and biofeedback are the most common psychological treatments used to treat migraine today. In spite of about 40 years of study and support from organizations throughout the world, which also involves US Headache Consortium and even the WHO and their other agencies, these therapies aren't officially approved for therapy in migraine sufferers in major nations around the world. In the early 2010s, the National Institute of Clinical Excellence (NICE), UK brought out a research advice for a practical randomized trial to be conducted to conclude the effectiveness of mental interventions for therapy of long-term headache-like episodes, which makes the way for long-term provisions. [8]

No significant effects were seen on depression and anxiety levels of the patient. Thus, psychological therapies help alleviate symptoms and reduce frequency of occurrence of headaches conclusively. [9]

Osteopathic Manipulation Therapies

Osteopathic Manipulation Technique is a non-invasive therapy approach that has little to no adverse effects on the patient . There are several forms of headaches. Osteopathic Manipulation Technique has been found to be very helpful with migraines, tension-type headaches, combat-related events, post-traumatic headache, sinusitis, tooth extraction, concussions, and other associated conditions. Osteopathic Manipulation Technique is a non-invasive therapy option for those who suffer from a variety of headaches to reduce its severity and prognosis. This treatment option is targeted to the patient's specific needs and is provided by certified and experienced osteopathic physicians around the world . This assessment of literature also identifies areas where more study is needed in the subject. [10]

In a systematic meta-analysis, spinal manipulation showed remarkably similar effects to amitriptyline in prophylaxis for migraine-like headaches. This effectiveness showed a sharp decline in case of tension-type associated conditions .

A 2017 review study with a sample size of 265 stated that, in contrast to several other alternate therapies applied, Osteopathic Manipulation significantly benefits the receiver in terms of severity, frequency and intensity of headaches then rest of the procedures conducted .

There is highly important tentative proof that OMT is useful in treatment of migraines and severe forms of other headache . Nevertheless, more demanding strategies and methodologies are required in future research to reinforce this data for better analysis and result .[11-14]

Integrative Medicine

Integrative medicine claims to treat the patient of migraine as a whole, combining mind-body-spirit with conventional medicine. It's a more wider concept used to treat patient with severe migraine [5]

Nutraceuticals include therapeutic dietary interventions like

1. vitamin D
2. magnesium
3. coenzyme Q, and
4. melatonin.

While previous research has shown magnesium, riboflavin, feverfew, and butterbur to be highly beneficial in migraine and headache treatment, new research suggests that vitamin D, melatonin and increased doses of vitamin B6 (80 mg) or folate 5 mg combos, along with the amalgamation of magnesium 112.5 mg, CoenzymeQ10 100 mg and also feverfew 100 mg may also be beneficial and effective in today's clinical setting.[15-18]

In migraine or severe headache , there are very minimal evidence of effectiveness for omega-3 fatty acids and hence of no use in pediatric population it only reduces the intensity of migraine in some cases and has little or no role in reducing inflammation and healing the endothelial or vascular injury. To guarantee better safety, butterbur must be devoid of pyrrolizidine alkaloids (PA), which are hepatotoxic in such cases . Acupuncture is better to fake acupuncture and even placebo, while therapy with physical focus (PT) endures to have lasting evidence of benefit in the patient.

With the exclusion of the fatal danger of cervical artery dismemberment with high-speed chiropractic management and liver toxicity with the PAs in butterbur, the adverse effects and hazards mentioned were limited and well endured generally. Several researches are being conducted throughout the world were more investigate mindfulness, physical therapy, exercise, melatonin, acupuncture, and chiropractic manipulation are done precisely .

The American Headache Society (AHS) and the American Academy of Neurology (AAN) are actively revising the strategies for better and integrated migraine management options, so more suggestions might be forthcoming shortly . [19-21]

Clinicians, neurologists, and specialists in today's scientific world may consider and incorporate these alternative interventions into their clinical practice more often as and when required for better treatment and fast relief or recovery of the critical , diagnosed cases and undiagnosed cases.

Placebo Therapies

Analgesia caused via placebo was always thought as a phenomena that was solely psychological. But however this is not recognized any longer in today's setting and is of no value . Nonetheless, psychological mechanisms are unquestionably important and are a healthy asset and two in very particular, the conditioning and expectation systems, need special emphasis in the established current scenario. The conditioning process, also known as the Pavlovian learning instrument, points to the habituated response in the migraine patient , meaning the ability of repeated benign stimulus or managements to elicit a reaction following divergences with active stimuli or treatments. In other terms, prior experience always impacts future results, and prior pain treatment reaction impacts impending analgesia.

The direct biological benefits of these therapies are small and very effective but raising issues about how the 'true value' of these and other medicines is determined, a recent meta-analysis of placebo-controlled trials using calcitonin gene-related peptide (CGRP) antibodies for migraine has found.

Conclusion:

Upon a very comprehensive , well evaluated and established exhaustive review of a vast body of clinical literature, we can now firmly and conclusively state that the treatment of headaches in pediatric populations is no longer restricted by a select few pharmacological options in today's clinical setting. The new-age alternative medicine, surgeries and its therapies are shown to be both safe and effective in the age-group of our interest. By means of this review of literature, the authors urge clinicians and pediatric practitioners alike to give due consideration to the array of integrative options at their disposal when treating in the clinical setting in today's scenario and for future references.

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:

1. Caviness V, Ebinger F. Chapter 86 - Headache in pediatric practice. In: Dulac O, Lassonde M, Sarnat HB, editors. Handbook of Clinical Neurology [Internet]. Elsevier; 2013 [cited 2021 Jul 17]. p. 827–38. (Pediatric Neurology Part II; vol. 112). Available from: <https://www.sciencedirect.com/science/article/pii/B9780444529107000027>
2. Faedda N, Cerutti R, Verdecchia P, Migliorini D, Arruda M, Guidetti V. Behavioral management of headache in children and adolescents. *J Headache Pain*. 2016 Sep 5;17(1):80pat
3. Sheridan D, Sun B, O'Brien P, Hansen M. Intravenous Sodium Valproate for Acute Pediatric Headache. *J Emerg Med*. 2015 Oct;49(4):541-5. doi: 10.1016/j.jemermed.2015.02.024. Epub 2015 May 16. PMID: 25986331.
4. Kabbouche M. Pediatric Inpatient Headache Therapy: What is Available. *Headache*. 2015 Nov-Dec;55(10):1426-9. doi: 10.1111/head.12701. Epub 2015 Oct 31. PMID: 26517974.
5. Yurekli, V.A., Akhan, G., Kutluhan, S. *et al*. The effect of sodium valproate on chronic daily headache and its subgroups. *J Headache Pain* 9, 37–41 (2008). <https://doi.org/10.1007/s10194-008-0002-5>
6. Lan L, Zhang X, Li X, Rong X, Peng Y. The efficacy of transcranial magnetic stimulation on migraine: a meta-analysis of randomized controlled trails. *J Headache Pain*. 2017;18(1):86. Published 2017 Aug 22. doi:10.1186/s10194-017-0792-4
7. Harris P, Loveman E, Clegg A, Easton S, Berry N. Systematic review of cognitive behavioural therapy for the management of headaches and migraines in adults. *Br J Pain*. 2015;9(4):213-224. doi:10.1177/2049463715578291.
8. Sullivan A, Cousins S, Ridsdale L. Psychological interventions for migraine: a systematic review. *J Neurol*. 2016;263(12):2369-2377. doi:10.1007/s00415-016-8126-z
9. Fisher E, Law E, Dudeney J, Palermo TM, Stewart G, Eccleston C. Psychological therapies for the management of chronic and recurrent pain in children and adolescents. *Cochrane Database Syst Rev*. 2018 Sep 1;2018(9):CD003subject
10. Whalen J, Yao S, Leder A. A Short Review of the Treatment of Headaches Using Osteopathic Manipulative Treatment. *Curr Pain Headache Rep*. 2018 Oct 5;22(12):82. doi: 10.1007/s11916-018-0736-y. PMID: 30291550.
11. Ghogare, Ajinkya Sureshrao, and Pradeep Shriram Patil. "A Cross-Sectional Study of Co-Morbid Generalized Anxiety Disorder and Major Depressive Disorder in Patients with Tension-Type Headache Attending Tertiary Health Care Centre in Central Rural India." *NIGERIAN POSTGRADUATE MEDICAL JOURNAL* 27, no. 3 (September 2020): 224–29. https://doi.org/10.4103/npmj.npmj_23_20.
12. Dhande, Nikhil, Sunil Kumar, and Ashwini Bolane. "Assessment of Psychosocial Distress among the Palliative Care Patients in Wardha District of Maharashtra." *INDIAN JOURNAL OF PALLIATIVE CARE* 26, no. 3 (September 2020): 302–5. https://doi.org/10.4103/IJPC.IJPC_114_19.

13. Nagdive, Amit, R. U. Zaman, Himanshu Deepak Mansharamani, Prakash B. Behere, and Rouchelle Fernandes. "A Study of Perceived Stress & Coping in Interns in a Tertiary Care Hospital in a North Eastern State of India." *JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS* 9, no. 52 (December 28, 2020): 3950–55. <https://doi.org/10.14260/jemds/2020/864>.
14. Somani, Ayush, Deep Hathi, Sourya Acharya, and Anusha Gupta. "Traumatic Rhabdomyolysis Presenting as Acute Kidney Injury and Acute Respiratory Distress Syndrome in Young Male Athlete." *MEDICAL SCIENCE* 24, no. 102 (April 2020): 771–75.
15. Nagdiv, Amit A. P. "A Study of Emotional Intelligence, Perceived Stress and Coping in Final Year Medical Undergraduates." *INDIAN JOURNAL OF PSYCHIATRY* 61, no. 9, 3 (January 2019): S464–65.
16. Salampurua, Shruti, Shubhada Jajoo, and Sourya Acharya. "Acute Respiratory Distress Syndrome during Pregnancy and Post-Partum - A Case Series with Spectrum of Near Miss to Mortality." *JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS* 8, no. 49 (December 9, 2019): 3724–26. <https://doi.org/10.14260/jemds/2019/806>.
17. Thakare, Seema H. "Assessment Of Role Of Diet, Life Style & Stress In The Etiopathogenesis Of Constipation In Geriatric Patients." *International Journal Of Modern Agriculture* 9, No. 3 (2020): 137–41.
18. Jha RK, Singh A, Koundal P, Ambad RS. Role of Lipid and Oxidative Stress in Psoriatic Patients - A Case Control Study. *JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS*. 2021 Jan 18;10(3):132–6.
19. Halani D, Jaiswal A, Kumar S, Talwar D, Madaan S. Post natal covid-19 induced severe acute respiratory distress syndrome managed with monoclonal antibody and prone ventilation. *MEDICAL SCIENCE*. 2021 Jun;25(112):1427–31.
20. Palkrit S, Naqvi WM, Burhani T. Physiotherapeutic Approach in Stress Urinary Incontinence with Prolapsed Uterus: A Case Report. *JOURNAL OF PHARMACEUTICAL RESEARCH INTERNATIONAL*. 2021;33(34A):54–9.
21. Suraj S, Prakash A, Dawande P, Noman O. Exploring the Pathogenic Role of Stress in Inflammatory Bowel Disease and its Management. *JOURNAL OF PHARMACEUTICAL RESEARCH INTERNATIONAL*. 2021;33(39A):17–22.