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Title: Management of Childhood Migraine by Headache Specialist versus Non-Headache Specialists

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Management of Childhood Migraine by Headache Specialist versus Non-Headache Specialists

Abstract

Objective: This study aims to compare the management practices of a headache specialist with non-headache specialists in the treatment of children with migraine. The use of appropriate rescue medications and prophylactic agents, application of neuro-imaging, and short-term outcomes are compared in children treated by the 2 groups of physicians.

Methods: A retrospective cohort study was conducted utilizing the electronic medical records of children 3-18 years of age with migraine, who were evaluated at a tertiary care children's hospital from 2016-2018.

Results: Of the 849 patients that met the study criteria, 469 children were classified as having chronic migraine or high- frequency episodic migraine *and* were followed up on at least one occasion by the neurologists. Imaging was obtained in 66.5% of all children with migraine. The headache specialist used 5-HT agonists ("triptans") for migraine management in 56.7% (76/135) of cases compared to non-headache specialists who prescribed them in 28.7% (96/334) of cases ($p < 0.001$). Of the children with chronic migraine, the headache specialist evaluated 135 patients while the non-headache specialists treated 334 children. Non-headache specialists prescribed prophylaxis in the form of natural supplements more frequently (63.8% of cases) compared to the headache specialist (38.5% of children) ($p<0.001$). On the other hand, prophylaxis with prescription drugs was utilized more often by headache specialist (66.7%) than non-headache specialists (37.4%) ($p<0.001$).

Conclusions: Imaging appears to be commonly recommended by both headache specialists and non-headache specialists in children with migraine. The headache specialist was more likely to use triptans as rescue medications for pediatric migraine. Outcomes in the short term were not statistically different whether children were being managed by the headache specialist or the non-headache specialists.

Introduction

Migraine is a common disorder in children, affecting 4% to 11% of those between 7 years and 11 years of age, and 8% to 23% of adolescents[1]. Since the disorder is widely prevalent, it would stand to reason that the bulk of care to children with migraine would be provided by primary care physicians, as it is in adults. Only a small percentage of adults with migraine are referred to a neurologist or headache specialist[2][3]. However, as medicine continues to become specialized, there is evidence that children with certain conditions, for example, epilepsy, who are evaluated at tertiary care centers have better outcomes[4].Similarly, there is some indication that adults who have access to a headache specialist can manage their symptoms more effectively and have greater satisfaction[5]. Use of appropriate rescue medications such as 5-hydroxytryptamine agonists (commonly referred to as triptans) seem to be more widely prescribed by neurologists[6]. On the whole, migraine is often under-diagnosed and therefore under-treated in various parts of the world[7].

The primary purpose of this study is to compare the management practices of child neurologists who are not headache specialists, with a pediatric headache specialist at a tertiary care children's hospital. We hypothesize, a priori, that the headache specialist would offer effective abortive options and start evidence-based prophylaxis, when indicated, at a higher rate. We propose that when care is provided by a headache specialist, there is more judicious use of neuroimaging. Finally, at short term follow-up, we propose that children evaluated in the headache clinic would have fewer headache days.

As a secondary objective, we aim to describe the demographics of the population referred for evaluation of migraine to a tertiary care institution.

Patients and Methods

A retrospective cohort study was conducted using the electronic records of children who were evaluated at the general neurology or headache clinics of the Children's Hospital of Michigan (Detroit, MI) from 2016- 2018. The total number of referrals to the outpatient neurology clinic is approximately 14,000 per year. The overwhelming majority of children who are evaluated in the neurology department are referred by their pediatricians, with very few parents requesting an appointment on their own. Prior to initiating the study, we obtained written approval from the Institutional Review Board of Wayne State University School of Medicine. Consent and Assent

was waived by the Institutional Review Board due to the retrospective nature of the study. This is a primary analysis of the data set with no prior publications available that report the results of this data set.

Study Setting

The department of child neurology at the study site consists of one headache specialist (LS) who runs a headache clinic in conjunction with mid-level providers and 8 child neurologists, who have other areas of expertise (non-headache specialists). Mid-level providers evaluate and treat patients solely under the guidance of the supervising physician. The general neurology clinics for purposes of this study are defined as those clinics staffed by the non-headache specialists. The headache specialist is board certified in Headache Medicine by the United Council of Neurologic Specialties. Patients are usually scheduled to be followed up 3 months after their initial visit. Due to a large number of referrals for headache, not all children are evaluated in the headache clinic. Whether the child is evaluated in the headache clinic or by a non-headache specialist depends on who referring physician requests, patient preference, and availability of appointment slots. For instance, the referring physician may request that the patient be seen at the earliest, in which case the child would most likely be scheduled with a non-headache specialist. In most instances, requests for evaluation of headache are not actively triaged by a nurse or physician. The headache specialist uses a structured template for evaluation and documentation.

Study Population

Children 3 years to 18 years of age who were evaluated at the Children's Hospital outpatient general neurology or headache clinics and given a primary diagnosis of migraine with aura, migraine without aura, or chronic migraine were included for analysis. Children with migraine variants, such as cyclical vomiting and abdominal migraine, were excluded. For descriptive analysis, we created a database of outpatient neurology visits that included the above diagnoses.

We examined the characteristics of the study cohort with respect to 1) patient demographics including age, gender, and race and residential status i.e. urban versus suburban. Postal zip codes which encompassed a 10-mile radius from the hospital and located within the city limits of Detroit were classified as urban, 2) clinical features including duration to seek a neurology consult and duration of symptoms prior to being referred to a neurologist. To give better context for our descriptive data, we also examined the most common comorbidities including obesity, snoring, seizures, and psychiatric conditions, such as attention deficit hyperactivity disorder and attention deficit disorder.

The ICHD-3 (International Classification of Headache Disorders) criteria were applied to establish a diagnosis of acute and chronic migraine. While ICD-9 codes were utilized to create the database, each record was reviewed individually by the research assistants and only those that met the ICHD-3 criteria for migraine were ultimately used in the study. In the event of ambiguity regarding the diagnosis or when a child had more than one type of headache, the headache specialist reviewed the record to establish a definitive diagnosis and decide whether to include the record in the database. Since some children were in the preschool age group, it was necessary to use the best judgment of the headache specialist to classify these children's symptoms as "most likely" to be migraine.

Comparisons between the treatment offered by the headache specialist and non-headache specialists focused on 3 variables: use of triptans, use of prophylactics which was dichotomized into nutraceuticals or prescription drugs (or both), and short term follow up outcomes using a single measure i.e. headache-free days.

Statistical Data Analysis

No statistical power calculation was conducted prior to the study. The sample size was based on the available data and the number of children who were evaluated at the study site during the study period that was agreed upon by the co-authors. The data is summarized and reported with categorical variables by numbers and percentages. The normality of continuous variables is tested by Shapiro-Wilk test. We described non-normally distributed continuous variables by Medians and Interquartile Ranges. Pearson's Chi-squared test was used to analyze the distribution of categorical variable by groups, provided no expected frequency less than 1, and no more than 20% of the cell should have an expected frequency less than 5, otherwise Fisher-Exact test is used for the analysis. SAS (version 9.4, SAS Institute Inc. Cary, North Carolina) was used to perform statistical analyses. Significance level was set at 0.05. A two -tail test was used to test the significance of null hypothesis for its rejection/acceptance at both side of the sampling distribution of test statistic. Cohen's Kappa of 0.70 was noted during tests of inter-rater reliability for categorical variables.

Results

The demographics of the study population and co-morbidities are listed in **Table 1**. Age ranges of the children who were analyzed is depicted in **Figure 1**. A total of 1215 electronic charts were available for review, of which 849 met the criteria for analysisand366 records were excluded due to inadequate documentation, not meeting ICHD criteria or being outside the age

range for the study. See **Figure 2** for flow diagram of the study sample. Out of the study sample of 849 records, 469 met the criteria for chronic migraine /high frequency episodic migraine *and* had at least one follow -up visit following the index visit. High frequency episodic migraine was defined as migraine that occurs less frequently (typically 10-14 headache days per month) than chronic migraine but nonetheless imposes significant disability on the individual.[8] While most studies of individuals with migraine have a female predominance, we had an almost equal proportion of males and females probably due to the fact that we included pre-pubertal children as well. We had a statistically equal representation of African-American, Caucasian, and children from "other" races in our cohort. There was also a statistically equal representation of children from urban and suburban locations

In our study group, 46.6% (395/849) of children were referred to the neurology department more than a year after the onset of migraine. About 19% of patients consulted with a neurologist between 6 months and 12 months (161/849), 9.2% (78/849) were evaluated by a neurologist between 4-6 months, and only in 17.5% (149/849) of cases was a consultation obtained in less than 4 months. With 7.5% (63/849) of patients, it was unknown how long it took to access a child neurologist after the onset of migraine as the parents and children could not recall the onset of symptoms. The time to see a headache specialist was not separately analyzed.

We compared the rate of imaging, treatment modalities, and outcomes for children who were treated by the headache specialist with those being treated by the non-headache specialists. The results of these findings are outlined in **Table 2.**

Imaging, in the form of MRI in almost all instances, was obtained in 66.5% (564/849) of all children with migraine. Of the children who had imaging, in 18.1% (102/564) of cases, it was ordered by the primary care physician. Normal imaging findings were noted in 59.2% (334/564) of cases who had an MRI, and incidental findings (arachnoid cysts, small pineal cysts, hypoplastic venous sinuses, developmental venous anomalies and small bright signals on T2 imaging) were noted in 37.9% (214/564) of children. Findings that would lead to a diagnosis other than migraine and considered clinically significant were noted in 2.4% (14/564). We considered bright signals on T2 to be an incidental finding as it has been described in individuals with migraine[9][10]. Children evaluated by a headache specialist received imaging at similar rates as those cared for by a non-headache specialist i.e. 68.9% vs. 74.2% (95%CI: -15.0%, 4.3%; p=0.238). None of the children with clinically significant findings on MRI had focal neurological findings such as papilledema, ataxia or cranial nerve palsies.

On the whole, triptans were prescribed in 30.3% (257/849) of all children in the study cohort. Children referred to the care of a headache specialist received triptans in 56.7% (76/135) of

cases compared to non-headache specialists who prescribed them in 28.7% (96/334) of cases (95%CI: 18.1%, 38.5%; p<0.001).

Of the total cohort of 849 patients, 469 children were diagnosed with chronic migraine/high frequency episodic migraine *and* evaluated two or more times by either the headache specialist or the non-headache specialists, i.e. an index visit and at least one follow-up visit. The headache specialist managed 135 patients while the non-headache specialists treated 334 children of the 469 children with chronic migraine/high frequency episodic headache. We did not include children who were initially evaluated by the non-headache specialist and were subsequently referred to the headache specialist. We did not match patients seen by the headache and non-headache specialist by age, gender, race or presence/absence of co-morbidities and most importantly severity of their disease. However, the 2 groups were fairly comparable with respect to demographics as can be seen in **Table 3** and **Table 4**. Of all children with chronic migraine/high frequency episodic migraine 82.1% (385/469) were started on prophylaxis after referral to the tertiary care hospital. In situations where prophylaxis was warranted (which in our center primarily includes chronic migraine or high-frequency migraine as defined above), the non-headache specialists started the patient on a daily regimen in 87.4% of cases (293/334), whereas the headache specialist prescribed prophylaxis at a rate of 91.8% (123/135) (p= 0.17). Prophylaxis in the form of natural supplements (most commonly riboflavin, butterbur, and coenzyme Q10) was preferred by the non-headache specialists 63.7% (212/334) vs. 38.7% (52/135) for the headache specialist (95%CI: -35.4%, -15%; p <0.001). On the other hand, prophylactic *drugs* were prescribed by the headache specialist in more instances (66.7% i.e. 90/135 vs. 37.4% i.e.125/334 with 95%CI: 19.2%, 39.3%; p<0.001). The most commonly used medication in children younger than 10 years of age was cyproheptadine. Children over the age of 10 years were prescribed topiramate, cyproheptadine, and amitriptyline, either individually or in combination, in most cases. A few children were treated by the headache specialist with lamotrigine, sodium valproate, propranolol, gabapentin and/or verapamil. At our center by consensus opinion, prophylaxis is usually started in children with chronic migraine or high frequency episodic migraine.

Finally, outcomes between children treated by the headache specialist versus the non-headache specialists were compared using a single parameter i.e. headache free days. Outcomes were classified as no improvement (less than 25% reduction in the frequency of headache days), mild to moderate improvement (25% to 50% reduction in the frequency of headache days), and significant improvement (more than 50% reduction in headache days). The mean follow-up period was 3 months since the first visit. No statistically significant

differences were noted in children evaluated by the headache specialist vs. non -headache specialist with respect in mild/moderate improvement or significant improvement in headache.

Discussion

We retrospectively analyzed the electronic health records of a sample of children with migraine who were referred for neurological evaluation to a tertiary care children's hospital.

Certain interesting patterns were noted in our cohort. First, it appears that about half of all children were referred more than a year after the onset of chronic migraine. While waiting for the neurology referral, less than 5% of children who qualified for the use of prophylactics were started on preventive medications. No child was prescribed a triptan by their primary care physician. While no clear data exists regarding who provides the bulk of care for children with migraine in the United States, a recent study of drug use in children with migraine suggests that slightly more than half of these children are cared for by pediatricians, about 25% receive care from a combination of family medicine and "other" physicians, and less than a quarter are treated by a neurologist[2]. Under-treatment of a migraine is widely prevalent, per reported literature, in both adults and children with a third of children with migraine receiving no prescription drugs during their neurology office visit[2]. It is thought that about 50% of individuals with migraine can self-manage their symptoms, with non-prescription drugs[11]. Those who fail over-the-counter medications would be the ones who benefit from prophylaxis and the use of more effective rescue medications. Even adults treated by headache specialists may be under treated with low access to rescue medications and prophylaxis. Adults who were seen by a specialist in Europe with migraine received a triptan in 4-20% of instances[12, 13]. A similar study in the United States by Lewis et al. noted that only 50% of children with chronic migraine who are eligible for prophylactic options, evaluated at a pediatric neurology clinic, received prophylaxis[14]. While one cannot conclude from the current study that outcomes were better for children who were treated by neurologists versus primary care physicians, it does appear that in our cohort, neurologists were proactive in utilizing prophylactic agents and using more effective rescue agents.

Secondly, imaging was obtained in about two-thirds of children, despite a diagnosis of migraine. It is well-documented that imaging is not helpful in the vast majority of children with a non-traumatic headache unless they have a focal neurological finding[15]. However, it appears that child neurologists have a low threshold for obtaining brain imaging, with imaging rates greater than pediatric emergency department physicians or primary care physicians[16]. In most instances, though it was rarely documented as such in the records, it appears that imaging was

obtained in our patients purely for parental concerns. The percentage of children with a concerning physical finding on examination or who experienced what was considered an atypical migraine pattern was less than 10% in our cohort. This rate of imaging is comparable to other studies wherein children with headache were evaluated by a neurologist[17]. Significant findings that necessitated a change in treatment plan were only found in 2.4 % of children, with a significant minority of children having incidental findings that did not influence treatment decisions. Our study reiterates that imaging is overused in the evaluation of a pediatric migraine, even by the very group of physicians who are involved in putting forth practice parameters that advise against it. Interestingly, there was no statistically significant difference in neuroimaging rates between the headache specialist and the non-headache specialists.

Comparison of Care Received from Non-Headache Specialist versus Headache Specialists

The most striking difference between treatment strategies employed by non-headache specialists versus the headache specialist was in the use of triptans. Non-headache specialists prescribed triptans 28.7% of the times while the headache specialist used it a frequency of 56.7%. Nonetheless, on the whole, only 30.3% of all children with migraine were prescribed a triptan.

Effective treatment of exacerbations is an important goal for patients and families. Non-steroidal anti-inflammatory drugs (NSAIDS) were widely used by children in our cohort prior to being evaluated by neurologists. Ibuprofen and acetaminophen are statistically more effective than placebo in children, have an acceptable side effect profile, and are easily accessible, thereby making them natural first-line drugs for abortive use[18]. However, serotonin 5-hydroxytryptamine agonists (“triptans”) are indicated for children who do not respond effectively to NSAIDS. Several triptans including rizatriptan and zolmatriptan have been studied in children as young as 6 years of age, are tolerated well in most instances, and offer relief in about 70% of children[19][20]. Aspirin and opiates were not used by any patients in our cohort. While the headache specialist utilized triptans more than the non-headache specialists, the lack of matching in terms of chronicity and intensity of symptoms between children evaluated by the 2 groups of physicians, precludes us from conclusively stating that the headache specialists used them more often because they were more aware of the indications. It does appears that the headache specialist in our study was more familiar with the indications for triptans in children and indeed offered them at significantly higher rates than non-headache specialists. However, even children being treated by the headache specialist were primarily prescribed oral sumatriptan that has low bioavailability and possibly low efficacy[21] [22]. The second-line triptan

used in our headache clinic was oral rizatriptan. These choices were determined by insurance coverage. Almotriptan and nasal zolmitriptan, which are FDA approved in adolescents, were not prescribed in any instance, even by the headache specialist.

Secondly, we compared preventive measures suggested to patients by both groups of neurology providers. On the whole prophylaxis was commenced in 82.1% of children with chronic migraine. Advice regarding lifestyle modifications, for example, hydration, sleep, exercise, and use of caffeine was equally offered to patients under the care of non-headache specialists and the headache specialist. There is evidence that all of the above play a modifying role in migraine pathogenesis[23)24)25)]. While management of a migraine in adults has been relatively well-defined by the American Academy of Neurology guidelines, first established in 2000, guidelines for the management of a pediatric migraine were established later with significant extrapolation from adult data[26,27)]. There was marked variation in the preventive treatment of migraine in children until the results of the CHAMP study in 2016 that provided high-quality evidence that placebo was comparable to use of commonly used prescription drugs[28)]. The lack of randomized controlled trials in children often leads to use of nutraceuticals or prescription drugs that lack high quality evidence to support their efficacy[29,30, 31)]. In our study the non-specialists favored natural supplements which may in fact be non-inferior to prescription drugs in children with chronic migraine[28)]

Short term follow-up noted no difference in outcomes as measured by a reduction in headache days between children treated by the headache specialist and those treated by non-headache specialists. We used a single measure to evaluate satisfaction with treatment and arbitrarily defined "mild-moderate" and "significant" improvement for purposes of this study. We used the documentation of the physician in the electronic records, which in turn depended on the recall bias of the child and the parents.

Limitations

We relied on documentation in the electronic medical record to assess why imaging was performed despite a reassuring clinical neurological examination and lack of atypical historical features. In most instances, the reason was not documented, which then by default was categorized as “imaging performed due to parental request”. We did not analyze if most imaging was obtained primarily in preschool age children. The incidence of incidental findings was higher than other studies involving children with a headache[32)].

In some instances, triptans were prescribed, but for reasons that were not clearly documented in the electronic record, the medication was not being used. Potential reasons may include lack of insurance coverage, parents' inability to obtain the medication or lack of knowledge regarding when to administer it to their child, or inability of the child to swallow medication in pill format (the only form approved for use in the bulk of our patients).

We did not analyze the short -term outcomes of children who received botulinum toxin, complementary treatments such as acupuncture/ cognitive behavior therapy, or those who used transcranial magnetic stimulation devices in addition to “standard” prophylactic agents.

Follow up of children who were being treated at the headache clinic versus the non-headache specialist clinic was conducted for an average period of 3 months, which may not be a sufficient length of time to study differences. Since an objective measure such as the PedMIDAS score or headache diary was not available in many instances, these measures that could have provided meaningful differences, could not be utilized as a comparative tool to study the 2 groups. The retrospective nature of the study and recollection bias further affects the results with respect to improvement in headache days.

Most importantly, this study confines itself to the experiences of a single center where the practice patterns of a single headache specialist are analyzed. There are inherent practice variations between headache specialists, depending on the location of their practice, individual training and most importantly due to lack of strong evidence favoring one drug over another with respect to prophylaxis. Therefore, the generalizability of the findings of the study is limited. We would especially like to highlight that children who were evaluated by the headache specialists vs. non-specialists were not matched with respect to duration or severity of symptoms and therefore the results must be interpreted in light of this limitation. Pooled experiences of pediatric headache specialists compared to non-headache specialists, across a variety of health care settings will be valuable in understanding care that is being provided to children with migraine.

Conclusions

We studied a sample of children with pediatric migraine and noted that referral to child neurology occurred after a year of the onset of symptoms in many cases. Imaging appears to be commonly recommended by both non-headache specialists and headache specialists in children with migraine, with little benefit in most instances. The headache specialist was more likely to use triptans, while non-headache specialists and the headache specialist started prophylaxis at similar rates in eligible participants. Outcomes in the short term, using limited

parameters, were not statistically different whether children were being managed by the headache specialist or the non-headache specialists.

We believe our study sample is representative of children referred to pediatric hospitals for management of migraine. Since not all children who are seen at tertiary care institutions are evaluated by pediatric headache specialists we sought to establish differences in treatment plans between the two groups of physicians. The generalizability of our study to larger groups of children, who receive care in a variety of medical settings is yet to be established.

REFERENCES

(1) Steward WF, Linet MS, Celentano DD, Van Natta M, Ziegler D. Age- and sexspecific incidence rates of migraine with and without visual aura. *Am J Epidemiol.* 1991;134(10):1111-1120.

(2) Lai LL, Koh L, Ho JA, Ting A, Obi A. Off-Label Prescribing for Children with Migraines in U.S. Ambulatory Care Settings. *J Manag Care Spec Pharm.* 2017 Mar;23(3):382-387.

(3)Lipton RB, Stewart WF. Migraine in the United States: a review of epidemiology and health care use. *Neurology* 1993; 43(suppl 3):S6–S10.

(4) Dwivedi R, Ramanujam B, Chandra PS, Sapra S, Gulati S, Kalaivani M, Garg A, Bal CS, Tripathi M, Dwivedi SN, Sagar R, Sarkar C, Tripathi M.Surgery for Drug-Resistant Epilepsy in Children. *N Engl J Med*. 2017;377(17):1639-1647.

(5) Katsarava Z, Mania M, Lampl C, Herberhold J, and Steiner TJ.Poor medical care for people with migraine in Europe – evidence from the Eurolight study. *J Headache Pain*. 2018; 19(1): 10.

(6) Hu, O'Donnell, Kunkel, Berger. Survey of migraineurs referred to headache specialists: care, satisfaction, and outcomes.*Neurology;* 2000; 55(1): 141-143.

(7) Katsarava Z, Steiner TJ. Neglected headache: ignorance, arrogance or insouciance? *Cephalalgia.* 2012 Oct ;32(14):1019-1020.

(8) Silberstein SD, Lee L, Gandhi K, Fitzgerald T, Bell J, Cohen JM. *Headache 2018*; 58(10): 1579-1592.

(9) Kim BS, Illes J, Kaplan RT, Reiss A and Atlas SW. Incidental Findings on Pediatric MR Images of the Brain. *AJNR Am J Neuroradiol*. 2002 Nov-Dec;23(10):1674-1677.

(10) Autti T, Raininko R, Vanhanen SL, Kallio M, Santavuori P. MRI of the normal brain from early childhood to middle age. I. Appearances on T2- and proton density-weighted images and occurrence of incidental high-signal foci. *Neuroradiology*. 1994 Nov;36(8):644-648.

(11)Steiner TJ, Antonaci F, Jensen R, Lainez MJA, Lanteri-Minet M, and Valade D. Recommendations for headache service organisation and delivery in *Europe J Headache Pain.* 2011 Aug; 12(4): 419–426.

(12) Frisk P, Sporrong SK, Ljunggren G, Wettermark B, von Euler M. Utilisation of prescription and over-the-counter triptans: a cross-sectional study in Stockholm, *Sweden.Eur J ClinPharmacol.* 2016 Jun;72(6):747-754.

(13) Lucas C, Géraud G, Valade D, Chautard MH, Lantéri-Minet M. Recognition and therapeutic management of migraine in 2004, in France: results of FRAMIG 3, a French nationwide population-based survey.*Headache.* 2006 May;46(5):715-725.

(14) Lewis DW, Diamond S, Scott D, Jones V. Prophylactic treatment of pediatric migraine. *Headache.* 2004 Mar;44(3):230-237.

(15) Lewis DW, Ashwal S, Dahl G, Dorbad D, Hirtz D, Prensky A, Jarjour I; Quality Standards Subcommittee of the American Academy of Neurology; Practice Committee of the Child Neurology Society. Practice parameter: evaluation of children and adolescents with recurrent headaches: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology. 2002* Aug;59(4):490-498.

(16) Cain MR, Arkilo D, Linabery AM, Kharbanda AB. Emergency Department Use of Neuroimaging in Children and Adolescents Presenting with Headache. *J Pediatr*2018;201:196-201.

(17)Yılmaz Ü, Çeleğen M, Yılmaz TS, Gürçınar M, Ünalp A. Childhood headaches and brain magnetic resonance imaging findings.*Eur J Paediatr Neurol. 2014 Mar*;18(2):163-170

(18) Rastogi RG, Borrero-Mejias C, Hickman C, Lewis KS, Little R. Management of Episodic Migraine in Children and Adolescents: a Practical Approach. *CurrNeurolNeurosci Rep. 2018 Oct;*18(12):103.

(19) Friedman G. Advances in paediatric migraine. *Paediatr Child Health. 2002* Apr; 7(4): 239–244.

(20) Linder SL. Subcutaneous sumatriptan in the clinical setting: the first 50 consecutive patients with acute migraine in a pediatric neurology office practice.*Headache. 1996* Jul-Aug;36(7):419-422.

(21) Fujita M, Sato K, Nishioka H, Sakai F. Oral sumatriptan for migraine in children and adolescents: a randomized, multicenter, placebo-controlled, parallel group study*. Cephalalgia.* 2014 Apr*; 3*4(5):365-375.

(22) HämäläinenM.Oral sumatriptan for the acute treatment of migraine in children and adolescents: yet another failed study*. Cephalalgia*. 2014 Apr;34(5):325-326.

(23)Bruni O, Galli F, GuidettiV.Sleep hygiene and migraine in children and adolescents*. Cephalalgia. 1999 Dec*;19 Suppl 25:57-59.

(24) Narin SO, Pinar L, Erbas D, Oztürk V, Idiman F. The effects of exercise and exercise-related changes in blood nitric oxide level on migraine headache*. ClinRehabil. 2003 Sep;*17(6):624-630.

(25) Spigt MG, Kuijper EC, Schayck CP, Troost J, Knipschild PG, Linssen VM, Knottnerus JA. Increasing the daily water intake for the prophylactic treatment of headache: a pilot trial *Eur J Neurol. 2005 Sep*;12(9):715-718.

(26) Silberstein SD. Practice parameter: Evidence-based guidelines for migraine headache (an evidence-based review) *Neurology Sep 2000*; 55 (6): 754-762.

(27) Lewis D, Ashwal S, Hershey A, Hirtz D, Yonker M, Silberstein S. Practice Parameter: Pharmacological treatment of migraine headache in children and adolescents. *Neurology Dec 2004*;63 (12): 2215-2224.

(28) Powers SW, Hershey AD, Coffey CS, Chamberlin LA, Ecklund DJ, Sullivan S,KlingnerEA,YankeyJW,Kashikar-Zuck SM, Korbee LL, Costigan ML, Riss HH, Porter LL, The Childhood and Adolescent Migraine Prevention (CHAMP) Study: A Report on Baseline Characteristics of Participants. *Headache. 2016 May*; 56(5): 859–870.

(29) Benemei S, De Logu F, Li Puma S, Marone IM, Coppi E, Ugolini F, Liedtke W, Pollastro F, Appendino G, Geppetti P, Materazzi S, Nassini R. The anti-migraine component of butterbur extracts, isopetasin, desensitizes peptidergic nociceptors by acting on TRPA1 cation channel. *British journal of pharmacology 2017*; 174(17), 2897-2911.

(30) Tepper SJ. Nutraceutical and Other Modalities for the Treatment of Headache. *Continuum (MinneapMinn). 2015 Aug*; 21(4 Headache): 973–989.

(31)Silberstein SD. Preventive Migraine Treatment. *Continuum (MinneapMinn). 2015 Aug*; 21(4 Headache): 973–989.

(32) Gupta SN, Gupta VS, and White AC. Spectrum of intracranial incidental findings on pediatric brain magnetic resonance imaging: What clinician should know? *World J ClinPediatr. 2016 Aug; 5*(3): 262–272.

Sociodemographic Features of All Children with Migraine N=849

Age	Mean- 10.5 ± 4.6	Median- 10.5 Lower Quartile 4.5 Upper Quartile 12.5 IQR 8.0		
Gender	Female 472 (55.6%)	Male 377 (44.4%)		
Race	Black 255 (30.0%)	White 307 (36.2%)	Hispanic 28 (3.3 %)	Other 259 (30.6%)
Zip Code[@]	Urban 213 (25.1%)	Suburban 636 (74.9%)		
Obesity	323 (38%)			
OSAS	63 (7.4%)			
Seizures	46 (5.4%)			
Psychiatric Comorbidity (Depression, Anxiety, ADHD)	95 (11.2%)			

Table 2 Comparison of Management practices between Headache Specialist and Non-Headache Specialists N=469

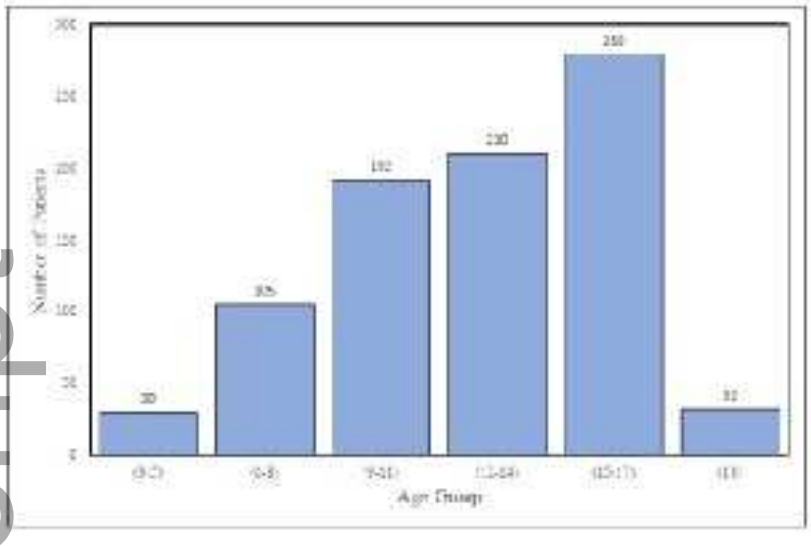
Treatment Variable		Headache Specialist (N=135)	General Neurologist (N=334)	P- value	95% CI for the Difference in Proportion
Imaging		93 (68. 9%)	248(74.2%)	0.238	(-15.0%, 4.3%)
Triptan Use		76 (56.7%)	96(28.7%)	< 0.001	(18.1%, 38.5%)
Use of Natural Supplement for Prophylaxis		52(38.7%)	212 (63.7%)	< 0.001	(-35.4%, -15%)
Use of Prescription Drugs for Prophylaxis		90 (66.7%)	125(37.4%)	<0.001	(19.2%, 39.3%)
Short Term Outcome of Treatment	No Significant improvement	36 (26.7%)	74(22.2%)	0.483	(-4.7%, 13.7%)
	Mild to Moderate Improvement	63 (46.7%)	150 (44.7%)		

Sociodemographic Features of Participants with Migraine Seen by Headache Specialist (N=133) and Non-Headache Specialists (N=334)

	Headache Specialist (N=133)	Non- Headache Specialist (N=334)	p-value	95 % CI for diff Mean/prop.
Age	Mean 12.8 ± 3.5 Median 14.0	Mean 12.2+3.6 Median 13.0	0.774	(-0.111, 1.313)
Gender (Female)	73 (54.8%)	189 (56.4%)	0.818	(-12.2%, 8.8%)
Race	**Black** 48 (36.1%)	**Black** 112 (33.8%)	0.676	(-7.6%, 1.27%)
	White 58 (43.6%)	**White** 141 (42.2%)	0.864	(-9.1%, 1.19%)
	Hispanic 6 (4.5%)	**Hispanic** 10 (3%)	0.595	(-3.0%, 6.0%)
	Others 21 (15.8%)	**Others** 71 (21.0%)	0.226	(-13%, 2.7%)
Obesity	46 (34.6%)	146 (43.7%)	0.088	(-19.3%, 1.1%)

OSAS	6 (4.5%)	30 (9.0%)	0.149	(4.5%, 0.7%)
Seizures	5 (3.8%)	24 (7.2%)	0.241	(-8%, 1.4%)
Psychiatric Conditions (Depression, Anxiety, ADHD)	10.5% (14/133)	13.8% (46/334)	0.428	(-10.2%, 3.7%)

AGE	HEADACHE SPECIALIST (N=133)	NON-SPECIALIST (N=334)	P-value
3-5 YEARS AGE	2 (1.5%)	9 (2.7%)	0.774
6-8 YEARS AGE	13 (9.8%)	43 (12.9%)	
9-11 YEARS AGE	32 (24.1%)	73 (21.9%)	
12-14 YEARS AGE	30 (22.6%)	76 (22.8%)	
15-17 YEARS AGE	46 (34.6%)	116 (34.7%)	
18-20 YEARS AGE	10 (7.5%)	17 (5.1%)	



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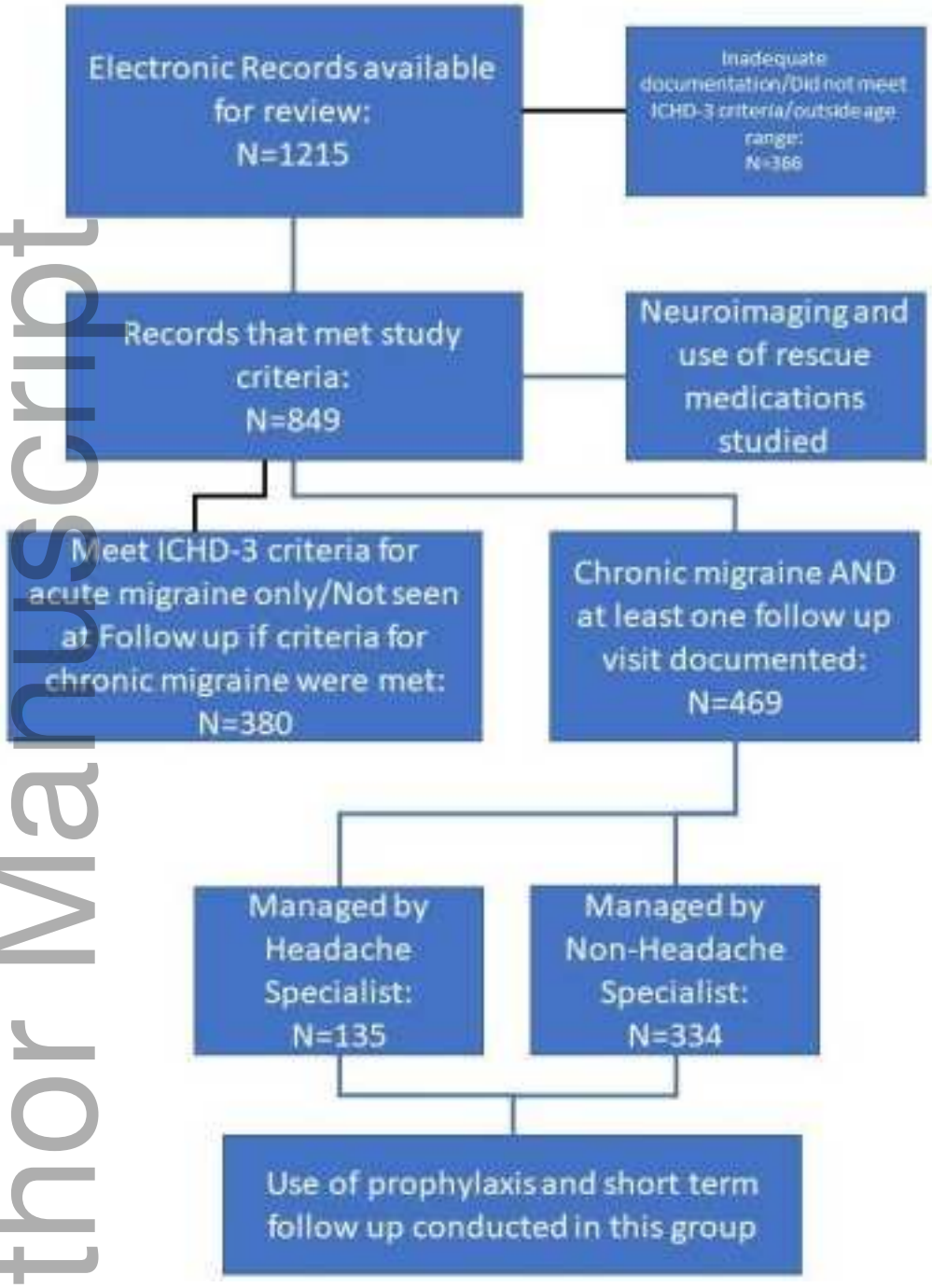

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