 doi:10.20944/preprints202012.0745.v1

Review

An evaluation of medication prescribing patterns for acute migraine in the emergency department: A scoping review

Jun Hua Lim [1], Leila Karimi [2] and Tissa Wijeratne [1,*]

[1] Department of Neurology, Western Hospital, Melbourne, VIC, Australia; Bowen.lim@wh.org.au
[2] School of Psychology and Public Health, La Trobe University, Melbourne, VIC, Australia; L.Karimi@latrobe.edu.au
[3] Department of Neurology, Western Hospital, Melbourne, VIC, Australia; tissa.wijeratne@wh.org.au
* Correspondence: tissa.wijeratne@wh.org.au , Tel.: +61393317297

Abstract: Migraine is one of the leading causes of disability worldwide [1,2] and patients with acute migraine frequently present to emergency departments (ED)[3]. The current literature suggests that ED treatment of migraine headache varies across institutions [4-7]. Considering this, we conducted a scoping review to summarize trends in medication prescribing patterns for acute migraine treatment in the ED setting. Trends were evaluated for factors influencing treatment choices, with particular attention placed on opioids and migraine specific therapy. This scoping review was based on the Arksey and O'Malley methodological framework[8] and included studies published between 1 January 2000 until 31 May 2020. 14 publications met the inclusion criteria. The most common classes of medication prescribed were often anti-emetics or Non-steroidal anti-inflammatory drugs (NSAID), but rates varied between studies. There was a concerning trend towards an underutilization of triptans and overutilization of opiates. The use of specific clinical goals of treatment (e.g. two-hour pain free freedom response) was also not evident. Additionally, 88% (n=8) of the 9 studies commenting on adherence to hospital or evidence-based guidelines stated that practices were non-adherent. Overall, the reviewed literature reveals treatment practices for acute migraine in the ED are heterogeneous and deviate from established international recommendations.

Keywords: Migraine, Acute care, Emergency department, analgesic, triptan, opioid and NSAID

1. Introduction

Migraine headaches are a common, debilitating, and costly neurological disorder. It affects up to 16.6% of the general population [5] and is recognized as the second most disabling condition in the world according to disability adjusted life years[1]. Beyond individual wellbeing and suffering, migraine is a public health issue that puts a burden on society through healthcare system costs and productivity costs. For example, in 2018 migraine cost the Australian economy $35.7 billion AUD in direct and indirect costs [9]. Global studies of the burden of migraine have reported similarly troubling numbers in Europe and the US[10-12].

Migraine sufferers often present to the emergency department (ED) seeking relief from their symptoms, with data from the United states showing at least 1.2 million presentations to the emergency department every year [3], and the ED is thought to provide 20% of migraine care [13]. These patients pose a treatment challenge for EDs as they sometimes have severe and/or prolonged not typical of their usual headache; and/or have tried their usual migraine treatment without success[14]. To add to the complexity, the available treatments for migraine are varied and may include paracetamol, antiemetics, nonsteroidal anti-inflammatory drugs (NSAIDs) as well as migraine specific therapies (ergots and triptans) and opiates. The complexity of migraine as a neurological disease is one of many reasons for heterogeneity in acute migraine treatment[15,16].

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2020 doi:10.20944/preprints202012.0745.v1

Evidence based recommendations for acute treatment of migraine headache in ED offer guidance and streamline management. Despite this, enumerable studies show deviation from these guidelines. Emergency departments typically adopt treatment choices conflicting with evidence-based guidelines, sometimes choosing suboptimal pharmacological treatment. For example, the practice of prescribing opiates for migraine is well documented in literature despite its association with chronification of migraine , development of medication overuse headache [17] and its propensity to harm patients through withdrawal or dependence [18,19].

Cross-institutional information regarding ED physician treatment practices for migraine is not well described in the current literature, and the amount of information currently available is unknown. For this reason, a scoping review was performed to map the current medication prescribing patterns and elucidate any gaps in knowledge in this area.

The current scoping review sought to answer the question: What are physician preferences for prescribing acute medication for the treatment of migraine in the ED? The scoping review was further guided by the following questions:

- What classes of medication were most frequently prescribed for the acute treatment of acute migraine in the ED?
- What are the rates which narcotic and migraine specific medications are prescribed in the ED?
- What factors influenced preferred treatment of migraine in the ED?
- What factors precluded adherence to evidence-based migraine guidelines?
- How can migraine treatment in ED be more consistent with current evidence-based guidelines?

After conducting this review, our results revealed that treatment practices for acute migraine in the ED are heterogeneous and deviate from established international recommendations. The trend of Triptan underutilization and opioid overutilization was pervasive and concerning.

2. Experimental Section

2.1. Eligibility criteria

2.1.1. Types of participants

The scoping review will consider any published studies on any patients over 18 presenting with migraine who presented to any emergency department. Studies in pregnant populations were excluded in this study due to a lack of generalizability

2.1.2 Concept

The concept of interest was the prescribing patterns for the treatment of acute migraine in the ED. To be included in this review papers needed to focus on describing patterns of medications used for migraine patients in the emergency department.

2.1.3 Types of studies

The types of studies considered for this review included: Peer-reviewed quantitative, mixed-methods, Cochrane systematic reviews and meta-analyses, conference abstracts and case studies.

We considered studies which aimed to quantitatively describe patterns of medication use for migraine patients. Migraine patients included those who were diagnosed with Migraine headache by a medical professional or based on the International classification of headache disorders (ICHD)

 doi:10.20944/preprints202012.0745.v1

migraine classification. Studies including those who were self-diagnosed with migraine or were not migraine specific (e.g. primary headache) were excluded.

2.2 Methods

Peer-reviewed journal papers were included if were relevant to the concept mentioned above, were published between 1/1/2000 until 5/31/2020, written in English and involved human subjects who were non-pregnant adults. This scoping review was conducted based on the Arksey and O'Malley methodological framework[20], and to identify all relevant publications for the current review the following three-step search strategy was used:

1. A search of MEDLINE, Cochrane and CINAHL was conducted, followed by an analysis of words contained in the title and abstract as well as index terms used to describe relevant articles.
2. All identified keywords and index terms were used to conduct a second search using the following databases: Ovid MEDLINE, Cochrane Library/Systematic Reviews, PubMed, CINAHL, PsycINFO and EMBASE.
3. A manual search as conducted to ensure all relevant studies were included

The following key words were used with the closest corresponding relevant subject headings: Migraine, acute care, emergency department, analgesic, triptan, opioid and NSAID. The search strategy was performed by the authors in conjunction with advice from an experienced librarian.

2.3 Screening and Data Extraction

The final search strategy results were exported into Endnote X9. The screening the web-based tool Covidence was used to aid the process of removing duplications, screening, and data extraction

3. Results

Our search strategy yielded 1302 studies, 818 remained for screening after duplicates were removed. The 818 studies underwent title and abstract screening. Following these 252 full text studies were assessed for eligibility. Of these studies 237 were excluded due to: Inappropriate outcomes, wrong study population, wrong study design, wrong setting and not meeting the inclusion criteria. This process resulted in 14 studies which were selected for inclusion in the current review. Figure 1 shows a PRISMA diagram depicting the publication screening and selection process

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2020 doi:10.20944/preprints202012.0745.v1

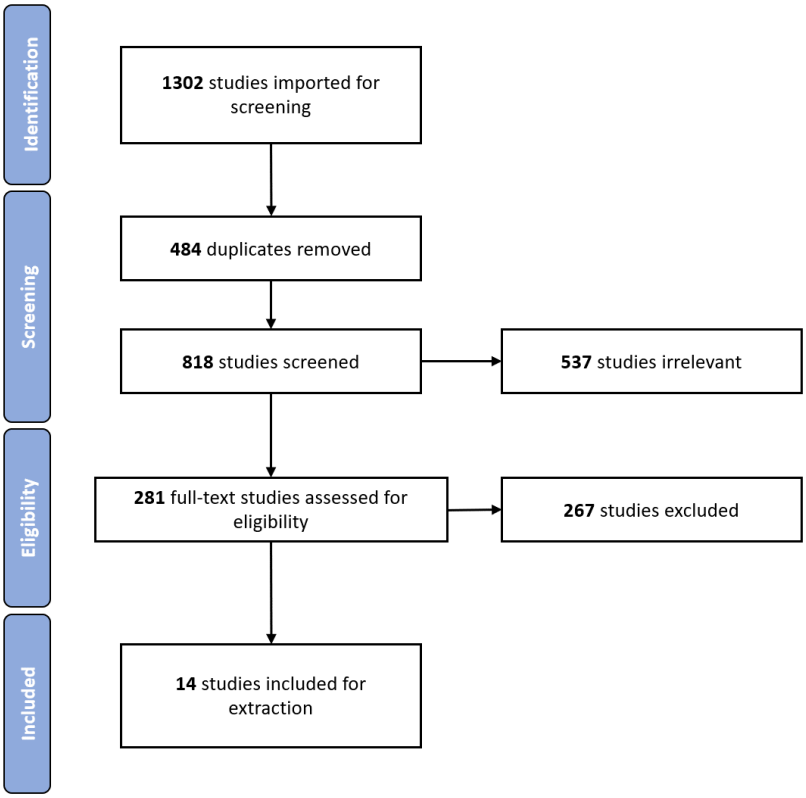

Figure 1. PRISMA flowchart indicating the publication screening and selection process.

3.1 Data screening and Results

The data screening process was jointly developed by the reviewers. A consensus was reached on which variables to extract and the extraction of data was performed by one reviewed then reviewed and agreed upon by another reviewer in situations of doubt.

Data from the included studies was extracted to address the review questions using the methods outlined by Peters *et al [21].* The extracted data included: basic article characteristics (e.g. author , year of publication and title), demographic information (subject population, age and gender) , study type (e.g. retrospective or prospective), main aim and outcomes, method for determining inclusion (e.g. use of international classification of diseases (ICD) coding, International Headache Society Classification (IHSC), or physician diagnosis of migraine , medications described (i.e. whether the study aimed to describe general prescription patterns or focused on comparing groups such as opioid vs non-opioid treatment), key findings (focused on the outcomes of the present review) and additional observations (focused other relevant outcomes not identified by this studies research focus). Some items extracted required interpretation by the reviewer, for instance in the outcomes section, reviewers may disagree on what outcomes are relevant to the main research question. A summary table of the article extraction is provided in Table 1.

Table 1[1]. Characteristics and summary results of included studies

Author	Title	Country and context	Main aim of the study	Study type	Study size	Age	Gender	Migraine population and definition	Medication	Key findings	Additional observations
Gunasekera, 2020 [22]	Overuse of opioids for acute migraine in an	St Vincent's Hospital, Melbourne,	To determine whether the ED prescribed medications	Retrospective cohort study.	744 patients	Mean age: 36.4 years	75% female	Patients admitted to St Vincent Hospital and	Manly opioids but also generalised prescribin	Polypharmacy was common for ED migraine management and was inconsistent with the national guidelines.	The most common reason for presenting to the ED with migraine was failed treatment at home (n=480 64.5%).

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2020 doi:10.20944/preprints202012.0745.v1

	Australian emergency department	Australia	consistent to the national guidelines.					diagnosed with a migraine based under the G439 ICD-10 code.	g patterns	Approximately 46.4% (n= 325) patients with a discharge diagnosis of migraine were treated with opioids, making it the most used medication to treat acute migraines. On the other hand, Triptans were underused for acute migraine management, treating only 6.9% (n=51) of patients. 60% (n=451) of patients were given antiemetics (e.g. metoclopramide, ondansetron and prochlorperazine) 51.8%(n=385) received paracetamol and 37% (n=274) where given NSAIDs(mostly ibuprofen).	Opioid containing medications were the most common choice of pre-hospital analgesic.
Mine n, 2020 [23]	A brief look at urgent care visits for migraine: the care received and ideas to guide migraine care in this proliferating medical setting	United States: 2 urgent care locations under New York University Langone Health System	To examine the treatment and management of migraine patients admitted in the ED, focusing on discrepancies between prescribed therapies and the American Headache Society migraine management guidelines.	A retrospective chart review of patients diagnosed with migraines	78 patients	Mean age: 32.5 years (SD: 8.1)	62 patients were female (79.5 %)	Patients diagnosed with migraines by physicians in NYU Langone Medhattan Urgent Care centre or NYU Langone Ambulatory Care West side Urgent care Centre	Generalised prescribing patterns	93.6% (n=73) of migraine patients had pain in ED. Only 12.3% (n=9) received acute migraine treatment medication within the ED consistent with American headache Society guidelines (IV metoclopramide) Of these patients 46.6% received no medication. Of those receiving medication ketorolac was the most common choice (70.6%). No patients received intravenous (IV sumatriptan or prochlorperazine Most patients were given prescriptions (78.2%, n=61) during their visit. 25.6% (n=20) received a prescription for triptans.	According to guidelines migraine patients should be treated with IV metoclopramide, IV prochlorperazine, and subcutaneous sumatriptan. These medications were not available in the pharmacy. However, only IV metoclopramide was found in the pharmacy
Shao, 2020 [24]	Patterns and predictors of opioid	United States: Datasets for ED patients	Main outcomes: (i) to describe the use of	This was a retrospective analysi	12,945 adult patients	Mean: 44.5 years	Female (85.9 %)	Patients enrolled for 6 months before or	Compared the use of opioid and non-opioi	Patients who arrived at the ED with a migraine were most often presented with five medications	After controlling for covariates , several predictors of index date opioid use were found this included:

	use among migraine patients at emergency departments: A retrospective database analysis	were collected from Baylor Scott & White Health, who run health services within Central Texas	opioid and non-opioid medication within migraine patients who were admitted into the emergency department (ii) compare demographics , clinical characteristics, past health resource utilization (HRU) and previous opiate use between opioid users and non-opioid users who presented to ED with a diagnosed with migraine (ii) identify predictors for opioid receipt at ED visits as a function of the aforementioned characteristics	s study which utilized electronic health records	presented with complaints due to migraine/headache. 788 met the inclusion criteria	old, majority, and white (76.1%).		after their ED visit who had one migraine related diagnostic coding (International Classification of Diseases, Ninth Revision (ICD-9): 346.xx or ICD-10: G43.xxx).	d medication. Also reported on antiemetics, opioids, non-opioid analgesics, antihistamines, and corticosteroids.	including antiemetics, opioids, non-opioid analgesics, antihistamines, and corticosteroids. 35.9% (n=283) of patients received opiates, the two most frequently used were morphine (n=103, 13.1%) and hydromorphone (n=85, 10.8%). 15% of patients were given opioid medication prescribed to them during their ED visit which needed to be filled at a pharmacy. Triptan use was minimal as only 3 patients (0.4%) received triptans in ED vend four patients (0.5%) were given triptans on discharge. Other common classes of drugs used during the index date ED visit included antiemetics (n=292, 37.1%), nonopioid analgesics (n=246, 31.2%), antihistamines (n=153, 19.4%), and corticosteroids (n=74, 9.4%). Adherence to the guidelines was minimal given the low triptan use and a high rate of opiate prescription (15%)	(i) previous migraine-related opioid use (odds ratio increased depending on amount of prescriptions from 1.66-4.43) (ii) non-migraine-related opioid use (10 or more prescriptions, Odds Ratio:1.93)(iii) previous all-cause ED visits (1–3 visits, Odds Ratio : 1.84) (iv) age (45–64 years, Odds Ratio:1.45) (v)patients with sleep disorder(Odds Ratio:1.43).
Ruzek, 2019 [25]	ED treatment of migraine patients has changed	United states: 4 new jersey Hospitals	How migraine treatment in the ED has changed between the years 1999-2000 and 2014. Secondary goal: If rates of migraine patients returning to ED in 72h changed	Multi-hospital retrospective cohort study	8046 migraine patients between 1999-2014 for examining 72 hr return 290 charts reviewed from 290 patients ((147 in	Mean 38 ± 12 years (chart review) Mean: 38 ± 13 years (72 h return)	89% were female (chart review) 84% were female (72 h return)	ED physician diagnosis of migraine coded with the respective ICD 9 code	Generalized prescribing patterns The following groups were assessed: parenteral narcotics, oral narcotics, antihistamines, and dopamine receptor antagonists prochlorperazine/metoclopramide (DRA).	There was more use of IV fluids (88%), Dopamine receptor antagonist (83%), ketorolac(38%), and dexamethasone(22%) in the 2014 cohort compared to 1999-2000 cohort. Moreover, narcotic prescription in Ed and on discharge was lower in the 2014 cohort compared to 2014 cohort. 8% (n=624) of all migraine patients between 1999- 2014 represented after 72h. The return rate was lower in 2014 (4%) compared to 1999-2000(12%), difference= 8%, 95% CI 5%–11%. The authors speculate that the increased use	Of the 2,824,710 patients presenting to ED, 0.28% or 8046 patients had migraine.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2020 doi:10.20944/preprints202012.0745.v1

					1999–2000 and 143 in 2014))					of non-narcotic medications contributed to the decrease	
Shao, 2017 [5]	The presenting and prescribing patterns of migraine in an Australian emergency department: A descriptive exploratory study	Queensland, Australia	To identify the varying demographics of patients which presented to the ED with a migraine and analyse the trends in medication treatments and prescriptions of the migraine.	Retrospective database interrogation of clinical records	2,228 patients	Mean age: 37.05 years (SD: 12.23 years) for migraine patients Mean age: 46.17 (SD 20.50) for total ED population	71% female (1578/2228)	Based on 2 criteria: a) ICD code primary of G43.9-migraine; and b) people who had presented to the ED using the word "migraine" as a description as a primary complaint.	Generalised prescribing patterns.	A variety of medications were used to treat migraine. Simple analgesics, anti-emetics and IV fluids with phenothiazine were commonly used. 20% of patients received oral or parenteral opiates (42 of 194 initial medication prescriptions, and 64 of 292 as required medication prescriptions). Opioid prescriptions were high despite the National Health and Medical Research Council's (NHMRC) guidelines recommending otherwise. Use of metoclopramide and phenothiazines were commonly prescribed for migraines and are consistent with NHMRC guidelines. Despite the triptans being recommended in the guidelines, its use within the ED was minimal.	The authors found that the proportion of ED patients presenting with migraine is steadily increasing. Additionally, the migraine population was trending towards younger patients (M=37.05, SD=13.23) than the whole ED population (M=46.17 SD=20.50) (P<0.001).
Young, 2017 [26]	Multicentre prevalence of opioid medication uses as abortive therapy in the ED treatment of migraine headaches	United states: 3 emergency departments in Connecticut	Main outcome: To determine the proportion of migraine patients who received opioid treatment. Other outcomes: Throughput measures (door to provider, door to medication and length	Retrospective cross-sectional analysis of consecutive adult emergency	1222 unique Visits, 931 unique patients	Median: 36 Years (Q1: 28, Q3:47)	82.7% Females	Based on ICD9 code for migraine or one of tis variations ICD9 code 346 or 346	Mainly opioids but also reported on NSAIDs, Antiemetics, muscle relaxants and other therapies	Opioids were given for migraine headache in 35.8% of the 1222 ED visits. Opioid prescription rates varied between centres. The rate of prescription ranged from 6.9%-69.9% depending on centre and rescue vs first-line therapy. 1 In assessing all categories of first line treatments medications the antiemetic category was most frequently used as first-line therapy at 35.3% of	Patients who received opioid treatment had a 37.7% increase in their length of stay compared to non-opioid treated counterparts [95% CI 1.207 to 1.617]). This patient group also required further treatment (rescue therapy) more compared to non-opioid treated counterparts (36.0% vs 25.1%, 95% CI 0.053 to 0.167)

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2020 doi:10.20944/preprints202012.0745.v1

			of stay) were recorded. Prevalence of non-opioid treatments groups were also noted							all orders, followed by NSAIDs at 16.0%, IV fluids at 13.3%, and opioids at 12.6%. Triptans were given to 1% of patients(n=2). An overreliance on opioids and underutilization of triptans suggests a strong deviation between real practice and guideline recommendations.	
Berberian, 2016 [27]	The utilization of narcotic analgesia in the treatment of migraine headaches	United States: an academic emergency department	To determine the frequency which parenteral narcotic analgesia is used to treat acute migraine in an academic ED and to compare the cost and length of stay between patients treated with narcotic vs non-narcotic treatments	Retrospective cohort study	421 subjects treated with parenteral agents from 521 records of patients diagnosed with migraine	Not stated	Not stated	Patients identified through EMR records through chief complaint and ICD9 codes for Migraine in 2013	Describing prescription of narcotic medication whist considering Parenteral medication only	32% (n=134) of patients were treated with one or more parenteral narcotic analgesic agents. The most used medications were antiemetics (92%), antihistamines (70%) and non-steroidal anti-inflammatory medications (62%).	When compared to their non-narcotic counterparts, the use of parenteral narcotics was associated with a longer length of stay (mean time 5:03 vs 4:06 minutes, P=0.001) but a reduced cost of say (mean cost $2363.62 vs $4528.82, P =0.00008) .
Cheng, 2016 [28]	Evaluation of the assessment and management of acute migraines in two Australian metropolitan emergency departments	Australia: The Alfred Hospital Emergency and Trauma Centre (E&TC) and Sandringham Hospital ED in Melbourne	To analyse the demographics, presentation, management, and outcomes of patients which presented to the ED with a migraine, making a comparison between first presenters and those with a history of migraine.	Retrospective cohort study	356 patients	Mean age: 37.8 years (SD 15.1)	74.8 % female	Patients were included if they met the following criteria: a) had a headache which had no organic cause; b) were discharged with a migraine diagnosis; and c) presented to the ED complaining of a "migraine"	Generalised prescribing patterns	The types of management in the ED were varied. However, except for the use of IV fluids and parenteral dopamine antagonists, migraine management was similar for patients with a previous history and first presenters. The initial migraine management included paracetamol in 48.8% of cases (n=178), NSAIDs (predominantly ibuprofen and aspirin) in 51.2% of cases (n=187). Migraine specific agents are used less frequently, triptans were used in 12.6% of cases (n=46) and ergots were used in 0.5% of cases (n=2). Opioids were given in 25.8% of cases (n=94)	First time presenters of migraine were investigated more thoroughly than patients with a previous history of migraines. CT scans of the brain were used in 34.5% of first-time presenters, and 10.4% of them were further assessed by inpatient teams, compared patients who had a history of migraines which were 22.9% and 8.8% respectively. The median length of stay in the ED was 4 (IQR 2–7) hours, with 163 (44.7%) patients admitted to the short-stay unit. A pain score of 5 or more was recorded at discharge in 31 (8.5%) patients. Those that required a short stay in the ED were often discharged

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2020 doi:10.20944/preprints202012.0745.v1

											from the hospital despite still having pain.
Friedman, 2014 [29]	Lack of evolution of Emergency Department treatment of migraine	United states: Randomly selected EDs	To make a comparison between the frequency of current medications given to patients with acute migraines in the US EDs with those used in 1998. The authors also aimed to identify factors related to the use of opioids	Retrospective study: Review of National Hospital Ambulatory Medical Care Survey (NHAMCS) data from 2010	1.2 million visits to the EDs in relation to migraine	Not stated	Not stated	Patients with a ICD9 coded discharge diagnosis of migraine	Generalised prescribing patterns	The author's analysis found that in 2010, opioids were administered in approximately 49% of ED visits (95%CI: 40, 58%). Parenteral Hydromorphone was a commonly used parenteral opioid in 2010 and was used in 25% (95%CI: 19, 33%) of visits, this is in stark contrast with 1998 where such practices were rare. Conversely the use of meperidine was more common in 1998 37% (29, 45%) , compared to 7% (4, 12%) in 2010.	Overall, women (53% [95%CI: 44, 63%](OR 0.44, 95%CI: 0.197, 0.995)) received opioids more often than men (34% [95%CI: 19, 52%]). Opioids as a treatment was also given less frequently to patents that had never visited the ED (41% [95%CI: 26, 58%]) compared to those that visited the ED 1-3 times per year (54% [95%CI: 40, 68%]) or more than 4 times annually (65% [95%CI: 43, 82%](OR for not at all versus 4 or more times : 0.37, 95%CI: 0.12, 1.1)).
Supapol, 2013 [30]	Assessing emergency department quality of migraine care in an Ontario Local Health Integrated Network(LHIN)	Canada: 12 Ontario EDs	To evaluate the prevalence of opioid therapy as a primary treatment for migraine headaches in 12 Ontario EDs by randomly selecting 100 migraine patient charts	Retrospective study	100 randomly selected studies	not stated	Not stated	Charts were selected based on the presence of National Ambulatory Care Reporting System (NACRS) most responsible diagnosis (MRDX) coding of migraine	Opioid prevalence	There was large amount of variation in opioid prescription rates as primary therapy for migraine. The proportion of patients treated at 6 of the 12 hospitals ranged from 0% (95% CI: 0-3.0) to 69% (59-77). In terms of adherence to standard therapy 6 of the 12 hospitals did not deviate significantly from the standard (0%-8% opiate prescription). The other 6 had proportions ranging from 24% to 69% which was not consistent with recommended treatment.	At two the hospitals where more than 60% of patients received opiate therapy, a small number of patients were responsible for 45% of migraine visits. Half of the hospitals in the LHIN met the standard for opioid primary therapy; 5% or less primary opioid therapy is an achievable goal.
Valade, 2011[31]	Migraine diagnosis and management in general emergency departments in France	France: 20 general emergency departments	Main outcomes: To determine the proportion of headache patients diagnosed with migraine. To ascertain demographic and	This study was a prospective, observational, national, multicentre study focusing on	15,835 patients were admitted to ED, 483 (3.1%) of patie	Mean: 37.6 Years +/-13.8	Female (74.5%)	ED physicians completed a questionnaire containing (1) the latest IHS criteria; (2) disease history	General prescribing patterns	Fewer than expected patients received migraine-specific prophylactic treatment or were encouraged to seek follow-up care. The most common treatment pharmacological treatment prescribed were non-opioid analgesics and	Upon discharge most patients (80.2% of 92 patients) did not experience a resolution of their migraine. Patients often received non-specific migraine medication upon discharge which did not help with symptoms. Upon follow up 36.3% of patients did not have

			clinical characteristics of these patients and describe the treatment and follow-up they received.	adults admitted within 20 general emergency departments throughout France during a period of one week.	nts had a headache while 98 (0.6%) had a migraine.			and treatment; (3) the reason for the emergency department visit; (4) whether further examination was required; and (5) treatment prescribed including prescription medicines at discharge.		NSAIDs respectively (61.2% and 42.9% of 98 patients with migraine) respectively. Triptans were given less often (11.2%). 9% of patients received no treatment Their results suggest potential for improved treatment choice, and they suggest awareness of guidelines is needed	complete resolution of their migraine after 48 hours. The study found that 1 in 5 patients with headaches were diagnosed with migraine. Common reasons to present to ED for migraine included a severe attack(49%) or ineffective treatment(20%)
Tornabene, 2009 [32]	Evaluating the use and timing of opioids for the treatment of migraine headaches in the emergency department	Two emergency departments associated with the University of California, Sandiego, USA	To examine and compare the treatment type and throughput times of migraine patients between an urban and suburban ED, and between patients that visited the ED multiple times (repeaters) vs only once (non-repeaters).	Retrospective review of ED patient records	189 patients (with 249 total visits) They were also looking at people who went into the ED once or more than once (repeaters vs non-repeaters)	Mean age of repeaters: 40.9 (SD 11.9) Mean age of non-repeaters: 39.5 (SD 10.6)	Repeater: 63.8% female Non-repeater: 75.8% female	Based on 2 criteria: a) ICD-9 classification and b) if patients were between 18-65 years and had an ED diagnosis described as a "migraine headache" or "migraine".	Compared opioids and non-opioid medications	68% of migraine patients in ED were treated with opioids. Within this group 81% were given opioids as their initial pharmacological treatment, and 38% received multiple doses.	Repeat patients who visited the ED multiple times were more likely to be treated with opioids compared to non-repeaters ,90.6% (n=87) vs 54.2%(n=83) respectively. Moreover repeat visitors were more likely to be given multiple doses of opiates (41.6%, n=40) compared to 15.7% of non-repeaters (n=24) In general, patients which received opioids stayed in the ED significantly longer, with opioid treated patients staying for 142 min (95% CI 124-160) while non-opioid treated patients stayed for 111min (95% CI 93-129) (p=0.015).
Wasay, 2006 [33]	Narcotic analgesics for acute migraine in the emergency room: are we meeting Headache Societies'	ER in Aga Khan University, Karachi, Pakistan	To discern whether IHS guidelines were being met within a tertiary care hospital ER in Pakistan.	Retrospective cohort study	161 patients	Mean age: 34 years	64% female	Applied IHS migraine criteria to all headache patients Migraine diagnosis based on the IHS criteria	Opioids vs non-opioids	This study found that opioid analgesics were used as first line migraine therapy in 24% of patients. The remaining patients (76%) were treated with non-opioid analgesics. Triptans were not available in this hospital setting however overall, it	After treatment, it was seen that 100 (62%) patients were discharged after being relieved of their pain, 50 (31%) patients were partially relieved, and 11 (7%) patients were still in pain after being discharged. The study found no relationship between pain relief and the administration

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2020 doi:10.20944/preprints202012.0745.v1

	guidelines?									concluded due to circumstances and a low rate of opioid use that the Aga Khan University ER did seem to be within the guidelines of the Headache Society. The authors acknowledge there is potential for further improvement.	of opioid vs non-opioid therapy.
Freidman,2009 [8]	Utilization, diagnosis, treatment, and cost of migraine treatment in the emergency department	United States: Strong Memorial Hospital or Highland Hospital ED	To determine the proportion of migraine patients presenting to ED who were treated with migraine-specific therapy as well as note the amount of unnecessary neuroimaging studies performed.	Retrospective cohort study of migraine ED visits	156 patients	Not stated	80.2 % female	The reliability of the coding migraine diagnoses was first assessed though 23 randomly selected from a pool of headache patients. Then patients with ICD 9 codes 346.0, 346.1, or 346.9 and a primary diagnosis of migraine were selected.	Migraine specific vs non migraine specific therapy	This study shows that migraine-specific treatment is underutilised in the ED. Of the 156 patients, a majority were treated with various parenteral antiemetics(n=95), narcotics (parenteral opioids, n=63; oral opioids n=19), or ketorolac(n=65). 78 patients (50%) had potential contraindications to receive migraine-specific therapy and justifying non-specific therapy. Of the 78 patients eligible for migraine-specific therapy, only 9 patients (11.5%) were able to receive migraine-specific therapy, while 10 patients received no treatment. Overall migraine specific therapy was underutilized, however patient eligibility for such therapy may explain this.	Out of the 156 patients, neuroimaging studies were conducted on 36 patients (23%), with only 4 patients not having a documented justification for obtaining the imaging study. The cost of radiology was a major factor to the overall financial burden of emergency care for migraine patients.

[1] Abbreviations: AHS, American Headache Society, CI Confidence interval , CT Computer Tomography , ED Emergency department , ICD International classification of diseases (IDC9 for 9th revision and ICD 10 for tenth revision), IHSC International headache society classification, IV Intravenous , IQR Interquartile range , NSAID Non-steroidal anti-inflammatory drug, NYU New York University, LHIN local Health integrated network SD Standard deviation , USA United states of America

The 14 Included publications were published between 2009 and 2020 with most studies from developed countries. This included: 57%(n=8) from the United States, 21%(n=3) from Australia and 7% (n=1) from Pakistan, France, and Canada. The study population with migraine ranged between 78 [23] and 2228 [5] subjects. Most migraineurs presenting to ED were young and female with average age ranges between 32.5 [23] and 44.5 [24] years and females consisting between 64% [33] and 85.9% of patients [24].

Of the 14 included publications all were cohort studies and used observation data, and all but one of the publications were retrospective [31]. Whilst each study made comments on prescribing patterns observed, the medication classes which they primarily focused on was different. About half (57%) of the publications focused on the use of opiates [22,24,26,27,30,32,33], about a third (35%)

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2020 doi:10.20944/preprints202012.0745.v1

sought to describe general prescribing patterns [5,23,25,28,29,31] without comparing specific classes of medications and only one study compared the use of migraine specific therapy to non-specific therapy [8].

Overall antiemetics as a general class were reported as the most used medication in 50% of studies[5,8,22,24-27], followed by non-opioid analgesics at 28.5% [23,28,31,33]. Intravenous fluids were the most commonly were reported therapy in 14% [5,25] of studies and 21% studies did not include detailed descriptions of non-opiate prescription patterns [29,30,32].

Regardless of the context of the studies, the comparisons of different pharmacologic treatments against opioid therapy was frequently raised. All extracted studies commenting on the consequences of patients who were prescribed opiates described poorer outcomes [26,27,32] or no increased pain relief [33]. Interestingly none of the studies mentioned concepts such as sustained pain free response or 2-hour pain freedom as a treatment goal. Suggesting opiates are being overprescribed to patients with migraine without any clear clinical goals of treatment.

The prescription of opiates to migraine patients has been a long-standing issue that has been described in literature for at least the last 10 years and the studies extracted here showed no discernible geographic trend in opioid prescriptions. Shao et al. (2017) illustrates the lack of geographic trends in their observations of opiate prescribing patterns in three hospitals in Connecticut USA, where they found that the rate of prescription of opiates varied from 6.9% to 69.9%. Friedman et al (2014) also agreed the with this sentiment, noting in their observations from multiple randomly sampled EDs across the United states, where they noted no observable geographic relationships between opiate prescription frequency according to geographic location or hospital type.

Regarding triptan prescription practices, of the extracted studies 2 noted that no IV triptans were used as they were not stocked in the pharmacy, an additional 2 studies noted that triptan prescription was under 1%. The highest rate of IV triptan use was noted by Freidman et al (2009), at 11.5% (n=9). Of the extracted studies describing triptan prescribing, only Freidman et al (2009) mentioned the proportion of eligible patients receiving triptans.

This raises the issue of non-compliance with evidence-based guidelines whether from the AHS or otherwise. Indeed, of the 9 studies which commented on adherence to hospital or clinical practice guidelines, 88% stated that their practices were non-adherent. The one study which commented that their ED practices were within the American headache society guidelines mentioned that there was room for improvement, as they used opioid analgesics for migraine 24% of the time.

4. Discussion

The current review attempted to characterize the treatment of migraine headaches in ED with a particular focus on opiate and triptan prescription patterns, rationalizations for medication choice and lack of adherence to evidence-based guidelines. The demographics in the included literature were consistent with published literature [4,34-36] where higher numbers of female migraineurs at younger ages were reported. Furthermore, our results revealed that anti-emetics and non-opioid analgesics (e.g. paracetamol or NSAIDs) were the most prescribed medications for migraines in ED. We also found that opiates continue to be overprescribed despite evidence of poor clinical outcomes. This occurs without any clearly defined clinical goals of treatment. A similar issue exists regarding triptan prescription. Intravenous sumatriptan is recommended by the American headache society guidelines [15] as a number of randomized controlled trials and systematic reviews have found that the triptan class are effective in the treatment of acute migraine[37]. Despite this recommendation, triptans were under prescribed. However, our results suggest the trend is potentially over reported due to lack of eligibility reporting.

The variation in opiate and triptan prescription rates suggests a lack of consistency in the ED approach to acute migraine management. More needs to be done to reduce opiate prescription and increase triptan use for eligible patients. Not only will these goals relieve the suffering of patients,

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2020 doi:10.20944/preprints202012.0745.v1

the extracted studies suggest that reducing opiate treatment may lessen the length of patient stays or representation to ED.

While the trend of opioid over prescription and triptan under prescription is clear, the extent of non-compliance with evidence-based medicine is unclear. To characterise the extent which opiate prescription, acceptable opiate use in accordance with AHS guidelines must be separated from unacceptable use of opiates. The AHS guidelines state classifies the use of intravenous opiates as 'May avoid- Level C'[15] and the American Academy of Neurology acknowledges that opioids are considered rescue therapy but should be used infrequently [17]. It is believed that a proper characterization of whether opiates were used as first line or rescue therapy is needed to make a complete judgement on the appropriate use of opiates within an institution. It is our opinion that to comply with best practice guidelines opiates an ED should have near zero levels of opiate as first-line therapy for migraine and opiates should not encompass the majority of rescue therapy prescriptions. We encourage future research to consider these details when conducting observational studies for opiate prescriptions in the ED.

The extent of triptan non-compliance is also unclear. Subcutaneous sumatriptan is given the highest level of evidence within the AHS guidelines, along with intravenous prochlorperazine and metoclopramide "should offer – level B". As mentioned previously the proportion of triptan eligible patients is not frequently reported. We suggest that those conducting observational studies on triptans versus other non-migraine specific treatments consider separating triptan eligible patients from ineligible patients to properly assess adherence. Implementing these measures may reduce the amount of triptans we can reasonably expect EDs to prescribe to be consistent with AHS guidelines.

The extracted papers rationalized non-adherence in different ways. As examples of rationalizations for overuse of opiates, Valade et al, 2010 suggested that ED doctors are not aware of treatment guidelines and may prescribe based on their preference or experience. As examples of rationalizations for low rates of triptan, Shao et al. 2020 suggested evidence that they are less effective in patients with late attacks may play a role. Additionally, given that sumatriptan is contraindicated in common conditions including cardiovascular disease and pregnancy the appropriateness of their use may narrower than we previously thought. Shao et al. 2020 also believed frequent occurrences of adverse effects in 50% of patients after triptan administration may lead physicians to avoid use. Comments made by Young et al. 2017 were also valid, they suggested that Individual factors such as previously reported poor response to triptans by patient, physician unfamiliarity with medication and high cost of triptans may also contribute to low use. The simplest action to take is to address the lack of awareness of evidence-based guidelines. Wasay et al. 2006 suggested that an education program in their ED may have reduced the tendency to prescribe opiates in their emergency department.

Finally, the last crucial issue to address variation from guidelines is the lack of availability of triptan medication. Wasay et al. 2006 (based in Pakistan) and Minen et al. 2020 (study based in the New York USA) reported that they had no access to intravenous triptan medication. It is important that EDs and hospital pharmacies stock IV triptans and dihydroergotamines to allow compliance with evidence-based medicines.

Future observational research into this area should focus on characterizing the extent which prescription patterns deviate from recommended guidelines. Specifically, whether opiates are being prescribed as first line treatment or rescue therapy and noting the eligibility of patient populations when commenting on levels of triptan therapy. Otherwise we believe that a prospective study on the effect of education regarding guidelines may be beneficial for improving for migraine treatment in ED.

4.1 Limitations

The current study only focused on quantitative studies where the primary aim was to describe medications prescription patterns. Our original objectives focusing on the rationale or factors precluding adherence to evidence-based guidelines was not directly addressed in many papers.

While we feel that our discussions are likely based on widely held beliefs in the field, due to the scope of our review there is a possibility that the opinions gathered may not be comprehensive. Furthermore, limiting the search to quantitative research may have excluded articles covering the qualitative aspects of non-adherence to recommended guidelines may have been missed. Finally, we may not have a global view of the issue, as many articles used in the review are from very highly developed countries. The ability to gain a global perspective on the issue is further hindered by only reviewing literature published in English. While a global may not have been achieved it is felt that the narrative that we provided here would be beneficial and translatable to many other contexts.

5. Conclusions

Overall, the current scoping review shows that there is a worrying tendency for the over prescription of opiates and under prescription of triptans. We observed a significant evidence-practice gap in the management of acute migraine in ED. The published papers continue to support the notion that migraine headaches continue to be the most neglected, worst respected, worst managed medical disorder in the world[2]. Ongoing advocacy, educational programs and translational research into this area should focus on addressing this issue as a matter of high priority.

Supplementary Materials:

Author Contributions: For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, T.W.; formal analysis, T.W., L.K. and J.L.; Investigation, J.L., L.K. and T.W; resources, T.W.; data curation J.L., L.K. and T.W; writing—original draft preparation, J.L.; writing—review and editing, J.L., L.K. and T.W.; visualization, L.K. , T.W. and J.L.; supervision, L.K. and T.W..; project administration, T.W.; All authors have read and agreed to the published version of the manuscript

Funding: This research received no external funding

Acknowledgments: None

Conflicts of Interest: The authors declare no conflict of interest

References

1. Group, G.B.D.N.D.C. Global, regional, and national burden of neurological disorders during 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Neurol* **2017**, *16*, 877-897, doi:10.1016/S1474-4422(17)30299-5.
2. Wijeratne, T.; Grisold, W.; Dodick, D.; Carroll, W. World Brain Day 2019: migraine, the painful truth. *Lancet Neurol* **2019**, *18*, 914, doi:10.1016/S1474-4422(19)30281-9.
3. Friedman, B.W.; West, J.; Vinson, D.R.; Minen, M.T.; Restivo, A.; Gallagher, E.J. Current management of migraine in US emergency departments: An analysis of the National Hospital Ambulatory Medical Care Survey. *Cephalalgia* **2015**, *35*, 301-309.
4. Kelly, A.M.; Knott, J.; Bennetts, S.; Huckson, S.; National Institute for Clinical Studies National Emergency Care Pain Management, P. Treatment of migraine in Australian Emergency Departments. *Emerg Med Australas* **2009**, *21*, 333-334, doi:10.1111/j.1742-6723.2009.01206.x.
5. Shao, E.; Hughes, J.; Eley, R. The presenting and prescribing patterns of migraine in an Australian emergency department: A descriptive exploratory study. *World J Emerg Med* **2017**, *8*, 170-176, doi:10.5847/wjem.j.1920-8642.2017.03.002.
6. Nijjar, S.S.; Pink, L.; Gordon, A.S. Examination of migraine management in emergency departments. *Pain Res Manag* **2011**, *16*, 183-186, doi:10.1155/2011/182867.
7. Morgenstern, L.B.; Huber, J.C.; Luna-Gonzales, H.; Saldin, K.R.; Grotta, J.C.; Shaw, S.G.; Knudson, L.; Frankowski, R.F. Headache in the emergency department. *Headache* **2001**, *41*, 537-541.
8. Friedman, D.; Feldon, S.; Holloway, R.; Fisher, S. Utilization, diagnosis, treatment and cost of migraine treatment in the emergency department. *Headache* **2009**, *49*, 1163-1173.
9. Report, D.A.E. Migraine in Australia Whitepaper. *Deloitte* **2018**.

10. 1Gustavsson, A.; Svensson, M.; Jacobi, F.; Allgulander, C.; Alonso, J.; Beghi, E.; Dodel, R.; Ekman, M.; Faravelli, C.; Fratiglioni, L., et al. Cost of disorders of the brain in Europe 2010. *Eur Neuropsychopharmacol* **2011**, *21*, 718-779, doi:10.1016/j.euroneuro.2011.08.008.
11. Olesen, J.; Gustavsson, A.; Svensson, M.; Wittchen, H.U.; Jonsson, B.; group, C.s.; European Brain, C. The economic cost of brain disorders in Europe. *Eur J Neurol* **2012**, *19*, 155-162, doi:10.1111/j.1468-1331.2011.03590.x.
12. Hawkins, K.; Wang, S.; Rupnow, M.F. Indirect cost burden of migraine in the United States. *J Occup Environ Med* **2007**, *49*, 368-374, doi:10.1097/JOM.0b013e31803b9510.
13. Schappert, S.M.; Rechtsteiner, E.A. Ambulatory medical care utilization estimates for 2006. *Natl Health Stat Report* **2008**, 1-29.
14. Diamond, M.; Cady, R. Initiating and optimizing acute therapy for migraine: the role of patient-centered stratified care. *Am J Med* **2005**, *118 Suppl 1*, 18S-27S, doi:10.1016/j.amjmed.2005.01.016.
15. Orr, S.L.; Friedman, B.W.; Christie, S.; Minen, M.T.; Bamford, C.; Kelley, N.E.; Tepper, D. Management of Adults With Acute Migraine in the Emergency Department: The American Headache Society Evidence Assessment of Parenteral Pharmacotherapies. *Headache* **2016**, *56*, 911-940, doi:10.1111/head.12835.
16. Marmura, M.J.; Silberstein, S.D.; Schwedt, T.J. The acute treatment of migraine in adults: the american headache society evidence assessment of migraine pharmacotherapies. *Headache* **2015**, *55*, 3-20, doi:10.1111/head.12499.
17. Langer-Gould, A.M.; Anderson, W.E.; Armstrong, M.J.; Cohen, A.B.; Eccher, M.A.; Iverson, D.J.; Potrebic, S.B.; Becker, A.; Larson, R.; Gedan, A., et al. The American Academy of Neurology's top five choosing wisely recommendations. *Neurology* **2013**, *81*, 1004-1011, doi:10.1212/WNL.0b013e31828aab14.
18. Gelfand, A.A.; Goadsby, P.J. A Neurologist's Guide to Acute Migraine Therapy in the Emergency Room. *The Neurohospitalist* **2012**, *2*, 51-59.
19. Bigal, M.E.; Serrano, D.; Buse, D.; Scher, A.; Stewart, W.F.; Lipton, R.B. Acute migraine medications and evolution from episodic to chronic migraine: a longitudinal population-based study. *Headache* **2008**, *48*, 1157-1168, doi:10.1111/j.1526-4610.2008.01217.x.
20. Arksey, H.; O'Malley, L. Scoping studies: towards a methodological framework. *International Journal of Social Research Methodology* **2005**, *8*, 19-32, doi:10.1080/1364557032000119616.
21. Khalil, H.; Peters, M.; Godfrey, C.M.; McInerney, P.; Soares, C.B.; Parker, D. An Evidence-Based Approach to Scoping Reviews. *Worldviews Evid Based Nurs* **2016**, *13*, 118-123, doi:10.1111/wvn.12144.
22. Gunasekera, L.; Akhlaghi, H.; Sun-Edelstein, C.; Heywood, J.; Sanders, L. Overuse of opioids for acute migraine in an Australian emergency department. *Emerg Med Australas* **2020**, *08*, 08, doi:10.1111/1742-6723.13504.
23. Minen, M.T.; Zhou, K.; Miller, L. A Brief Look at Urgent Care Visits for Migraine: The Care Received and Ideas to Guide Migraine Care in this Proliferating Medical Setting. *Headache* **2020**, *60*, 542-552, doi:10.1111/head.13717.
24. Shao, Q.; Rascati, K.L.; Lawson, K.A.; Wilson, J.P. Patterns and predictors of opioid use among migraine patients at emergency departments: A retrospective database analysis. *Cephalalgia.* **2020**.
25. Ruzek, M.; Richman, P.; Eskin, B.; Allegra, J.R. ED treatment of migraine patients has changed. *American Journal of Emergency Medicine* **2019**, *37*, 1069-1072, doi:10.1016/j.ajem.2018.08.051.
26. Young, N.; Silverman, D.; Bradford, H.; Finkelstein, J. Multicenter prevalence of opioid medication use as abortive therapy in the ED treatment of migraine headaches. *Am J Emerg Med* **2017**, *35*, 1845-1849, doi:10.1016/j.ajem.2017.06.015.
27. Berberian, J.; Fischer, M. The utilization of narcotic analgesia in the treatment of migraine headaches. *Academic Emergency Medicine* **2016**, *23*, S162-S163.
28. Cheng, C.T.; Law, G.T.W.M.; Roman, C.; Tan, G.; Mitra, B. Evaluation of the assessment and management of acute migraines in two Australian metropolitan emergency departments. *Journal of Emergency Medicine, Trauma and Acute Care* **2016**, *2016*.
29. Friedman, B.; West, J. Lack of evolution of Emergency Department treatment of migraine. *Journal of Pain* **2014**, *15*, S10.
30. Supapol, W.; Ackerman, M.; Worster, A. Assessing emergency department quality of migraine care in an Ontario Local Health Integrated Network. *Canadian Journal of Emergency Medicine* **2013**, *15 (Suppl 1)*, S9.
31. Valade, D.; Lucas, C.; Calvel, L.; Plaisance, P.; Derouet, N.; Meric, G.; Lanteri-Minet, M.; Giroud, M. Migraine diagnosis and management in general emergency departments in France. *Cephalalgia* **2011**, *31*, 471-480, doi:10.1177/0333102410378178.

32. Tornabene, S.V.; Deutsch, R.; Davis, D.P.; Chan, T.C.; Vilke, G.M. Evaluating the use and timing of opioids for the treatment of migraine headaches in the emergency department. *J Emerg Med* **2009**, *36*, 333-337, doi:10.1016/j.jemermed.2007.07.068.
33. Wasay, M.; Zaki, K.S.; Khan, S.U.; Rehmani, R. Narcotic analgesics for acute migraine in the emergency room: are we meeting Headache Societies' guidelines? *Journal of Headache & Pain* **2006**, *7*, 413-415.
34. Lipton, R.B.; Bigal, M.E.; Diamond, M.; Freitag, F.; Reed, M.L.; Stewart, W.F.; Group, A.A. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology* **2007**, *68*, 343-349, doi:10.1212/01.wnl.0000252808.97649.21.
35. Reuter, U. GBD 2016: still no improvement in the burden of migraine. *Lancet Neurol* **2018**, *17*, 929-930, doi:10.1016/S1474-4422(18)30360-0.
36. Karimi, L.; Crewther, S.G.; Wijeratne, T.; Evans, A.E.; Afshari, L.; Khalil, H. The Prevalence of Migraine With Anxiety Among Genders. *Frontiers in neurology* **2020**, *11*, 569405-569405, doi:10.3389/fneur.2020.569405.
37. Pringsheim, T.; Becker, W.J. Triptans for symptomatic treatment of migraine headache. *BMJ* **2014**, *348*, g2285, doi:10.1136/bmj.g2285.