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Overuse of opioids for acute migraine in an Australian emergency department

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The overuse of opioids for acute migraine in an Australian Emergency Department.

ABSTRACT:

Background and aims: Acute migraine is associated with significant personal, economic and work-related disability. Management guidelines advise use of simple analgesia, triptans, chlorpromazine and anti-emetics based on severity, with avoidance of opioids. We aimed to determine consistency of prescribing patterns in our ED with national guidelines.

Methods: We performed a retrospective cohort analysis of migraine presentations (ICD-10-AM G439) between 2012-2016. Exclusion criteria included migraine without headache, other primary headaches and secondary headaches. Demographic and prescribing data were extracted from medical records. Results have been reported as proportions.

Results: Of 4769 headache presentations, application of exclusion criteria led to a total of 744 patients who received a migraine diagnosis (G439). Most were female (558/744, 75%), young (mean age 36.4) and had a self-reported migraine history (558/744, 75%). There were 54 different medications prescribed. Paracetamol was more frequently prescribed (385/744, 52%) than aspirin (134/744, 18%). Opioid prescription occurred in nearly half of all presentations (345/744, 46%). Similar opioid prescriptions were also observed in those with a documented history of migraines (253/558, 45%). A minority of patients received triptans (51/744, 7%). Overall, a quarter of patients (189/744, 25%) received no guideline-recommended medications.

Conclusion: We observed considerable polypharmacy in ED migraine management with inconsistent prescribing patterns. Recommended medications were infrequently used and opioid use was common. Factors influencing prescribing patterns require further investigation in order to improve rates of guideline recommended treatment.

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Headache, Migraine Disorders, Acute Pain, Emergency Services, Hospital, Pain Management

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INTRODUCTION:

Headache is a common condition affecting nearly half of the general population[1]. Migraine, one common headache type, affects 18% of women and 6% of men during a lifespan.[2,3] It is among the top 20 causes of disability worldwide for both sexes and causes considerable disruptions to social life, relationships, employment and finances.[4,5,6] To compound the burden, most migraineurs are 25-55 years old and thus are affected adversely during key formative years in child-rearing and career development.[5,6,7]

Some patients present to the Emergency Department (ED) for relief of severe symptoms. Data from the United States reveal that head pain is the fifth leading cause of all ED visits, comprising 4 million visits annually[7]. Due to this high case burden, accurate migraine diagnosis and treatment is an essential skillset for ED physicians. Despite affecting 1 in 10 adults, studies suggest that migraine is under-estimated and under-treated in EDs worldwide.[3,6]

There are limited data regarding migraine management in Australian EDs. Only three such studies exist to date. Two studies, almost a decade apart, found that there was wide heterogeneity in prescriptions for acute migraine, with low rates of triptan use and common opioid prescription.[8,9] This finding was confirmed in a more recent Australian study which investigated prescription differences between first and repeat presentations to ED with migraine; it concluded that first time presentations are

investigated more heavily but did not receive any significantly different prescriptions.[10]

Australian guidelines for acute migraine management were released in 2006 by the National Health and Medical Research Council (NHMRC) with the 2011 publication rescinded in 2017.[11] It recommended treating mild migraine with aspirin and metoclopramide, while moderate-severe migraine could be treated with one of prochloperazine, chlorpromazine or sumatriptan.

Different recommendations are available via *Therapeutic Guidelines Limited*.[12] These guidelines recommend that first line treatment can be any of: aspirin, NSAIDs or paracetamol. It recommends anti-emetics where simple analgesics fail or where vomiting is prominent. Second line treatment are triptans. In severe cases, chlorpromazine and dihydroergotamine are advised as per 2017 guidelines, despite the latter medication being discontinued in Australia since 2012.[12] The various therapeutic options for acute migraine advised by both the NHMRC guidelines and *Therapeutic Guidelines Limited* have a strong evidence base for their use, and is supported by the recent 2018 American Headache Society Position Statement regarding therapeutics in migraine management[13].

Both *Therapeutic Guidelines Limited* and NHMRC guidelines discourage opioid use. Opioid use is associated with migraine chronification, poor response to both preventative and abortive therapy, increased ED lengths of stay, as well as medication-overuse headache, withdrawal and dependence.[14-20]

Our aim was to ascertain the extent of concordance between prescriptions for a discharge diagnosis of acute migraine against national prescribing guidelines, in order to understand how appropriately acute migraine is managed in an emergency setting.

METHODS:

This is a retrospective cohort study of patients receiving an ED diagnosis of migraine at St Vincent's Hospital Melbourne (SVHM). SVHM is a public tertiary centre that is affiliated with The University of Melbourne. SVHM has 880 beds and in 2015, had 42,534 emergency presentations and 199,521 outpatient appointments. There was no hospital or emergency policy regarding migraine management during this study.

The Patient Administration System was used to generate a report of patients presenting to the SVHM ED from January 1st 2012 to December 31st 2016. Records of all patients with a headache presentation receiving a migraine diagnosis under the G439 ICD-10 code were reviewed. Exclusion criteria were other primary headaches, secondary headaches, migraine without headache presentation and departure before medical assessment. We specifically did not evaluate the diagnosis of migraine against International Headache Society diagnostic criteria. The aim of the study was to conduct a real world evaluation of the appropriateness of management for the *working diagnosis* assigned by the treating clinician, irrespective of the diagnostic accuracy.

For each patient, data was extracted from electronic ED medical records and drug charts to obtain patient demographics, mode of arrival to ED, prescriptions, patient allergies, and follow-up recommendations. All data was extracted and checked twice for accuracy solely by the principal author and no discrepancy was found. Where data was not documented, such as migraine history, it was assumed that such a history was absent. Results were coded, imported into STATA (version 12) for analysis and results reported as proportions. The methodology for this project was reviewed and approved (QA 039/17).

RESULTS:

There were 4769 headache presentations to the emergency department between 1st of January, 2012 till 31st of December, 2016. Less than a quarter of these (1076/ 4769, 22.6%) received a discharge diagnosis of migraine (G439). Overall, only 748 patients (748/4769, 15.6%) with a diagnosis of migraine (G439) presented with a headache. Four patients were excluded due to departure prior to completion of medical assessment. In total, 744 patients with a headache presentation of migraine (G439) were analysed.

Demographic analysis of the presenting population shows that the majority of patients were female (558/744, 75%), Australian-born (501/744, 67%) and young (range between 15 to 87 years with mean age 36.4 years, standard deviation 13.4 years). Most self reported a prior migraine diagnosis (558/744, 75%).

A quarter of patients (189/744, 25%) arrived via ambulance, while the majority self-presented (555/744, 75%).

Most self-referred to ED (656/744, 88.0%), while GP referrals formed a small portion of arrivals (70/744, 9.4%). Referrals from other hospitals and internal hospital referrals formed the remaining 2.4% (18/744). In addition, 147 patients (19.8%) had seen a GP prior to arrival, although 430 (58.0%) did not have this information recorded.

Blood investigations included: full blood exam (479/744, 64.0%), biochemistry (478/744, 64.0%), coagulation studies (82/744, 11.0%), Beta-HCG (52/744, 7.0%) and thyroid function tests (23.0, 3.1%). Neuroimaging was used in 18.5% (138/744). CT brain was ordered in 133 (17.9%), while MRI brain were ordered in 5 patients (0.7%). No patient received both CT and MRI imaging. None of the patients receiving neuroimaging returned abnormal imaging results. Lumbar puncture was performed for 21 patients (2.8%) to exclude a secondary cause.

Most had failed self-medication at home (480/744, 64.5%). The treatments attempted prior to arrival are seen in supplementary table 1. The most common pre-hospital analgesic choices were opioid-containing medications (187/744, 25%).

There were 54 different medications prescribed for acute migraine during the study period (Table 1) demonstrating considerable polypharmacy and heterogeneity. Paracetamol was prescribed more commonly than the recommended simple analgesic aspirin. Triptans were used infrequently while opioids were prescribed in nearly half of all presentations. Chlorpromazine was the most widely used of all recommended medications. Use of guideline-recommended anti-emetics was low.

Over half of all patients (481/744, 64.7%) received intravenous fluids. Documented allergies to recommended treatments were 17% with half of them to opioids (9%).

The use of opioids did not differ significantly between those with and without a self-reported history of migraines. Overall, 75% of patients (558/744) had documented history of migraines and of these, nearly half (253/558, 45%) received opioids. In those without a documented migraine history (186/744, 25%), also nearly half (92/186, 49%) received opioids.

Half the patients were discharged home after ED consultation, 48% were admitted to the short-stay unit and 2% were admitted to the ward. There was no documented follow up for over a third of patients (259/744, 34.8%). Roughly a third of patients

were documented to follow up with GP (248/744, 33%), while neurology clinic referrals were made for much fewer (98/744, 13%).

DISCUSSION:

We present a real-world analysis of prescribing practices for a discharge diagnosis of acute migraine compared with national prescribing guidelines. Our study has revealed the persistent mismanagement of acute migraine despite copious evidence regarding evidence-based management in the acute setting[11-14]. Our results indicate persistent polypharmacy, over-use of opioids and marked underuse of triptans.

Our study period of 5 years, in addition to two previous 12-month and one 3 year study,[8,9,10] strengthens our understanding of ED prescribing patterns over time. Our findings add to the existing international literature regarding the need for improvement in acute migraine management in EDs worldwide,[3,6] with similarities in findings suggesting that a common approach to improvement strategies may be possible.

Overall, three quarters of patients received at least one guideline-recommended treatment. This is a significant improvement from the first Australian study in emergency migraine care in 2009 which showed that only 36% of patients received guideline recommended treatment.[8] However, our study still found that over a quarter of patients did not receive any guideline-accepted medications. It is unclear to what extent contraindications, allergies, lack of knowledge about appropriate abortive therapies or physician preferences contributed to these observed practices. This is concerning as under-treatment of acute migraine can lead to migraine chronification and repeat ED presentations; further targeted interventions to address migraine management is required.

In this study, paracetamol was more commonly given than aspirin. Anti-emetics were also under-used with prochloperazine and metoclopramide prescribed in less than half of patients. The use of anti-emetics in migraine treatment is important in countering nausea, vomiting and migraine-induced gastric stasis, thus aiding the absorption of oral medication such as aspirin.[13,14] Furthermore, the recommended anti-emetics also have anti-headache properties which can be conducive to migraine relief.[14]

Chlorpromazine was the most widely used of all guideline-recommended medication, while triptans were the least frequently prescribed. The wide use of chlorpromazine may be due to familiarity of emergency physicians with the medication, severity of headache on presentation, previous successful treatment with this or its sedative effects. Its intravenous route of administration may also be preferable to the myriad routes available for triptans including subcutaneous and inhaled forms, possibly decreasing confidence in its use. However, this is impossible to conclude without a prospective study.

It is possible that opioids are preferred to triptans by ED physicians as opioid use is common, leading to greater confidence in its use. Interestingly, in nearly half of all patients who had tried triptans at home, opioids were given in the ED raising the possibility of over-reliance on opioids where initial therapy fails. In this hospital, opioid prescription is solely physician-driven and the fact that nearly 1 in 2 migraine patients received opioids upon presentation should be addressed as a priority. Nurse-initiated paracetamol exists in this institution and its initial failure may be a reason for high opioid prescription, whereby doctors in ED ‘treat on the run’ without a patient review in order to alleviate patient pain. A prospective study to examine this further would be important in discouraging such a trend.

Our finding that opioids were given to roughly 50% of patients with a discharge diagnosis of migraine and with a documented history of migraines suggests that this

past history may not be taken into account when evaluating the current episode. It must be noted that this retrospective analysis may mean some patients with a history of migraines did not have this information documented, further underestimating the extent of opioid prescriptions in known migraineurs. Other possible reasons may include lack of education regarding appropriate management of acute migraine or barriers to its implementation. However, the use of lumbar punctures and radiology in our population suggests that the initial headache presentation may have been undifferentiated, leading to opioid use which retrospectively, was detrimental when the ultimate diagnosis was migraine. Furthermore, use of opioids where there was no prior migraine history or once initial investigations were normal may be appropriate 2nd line therapy especially whilst awaiting investigations or response to treatment.

Our presenting population was predominantly young females, similar to findings from international studies.[5,6] However, unlike previous studies suggesting that many migraineurs present to ED without attempting any analgesia,[21] two thirds of our presenting population presented after failed analgesia at home. Opioids were the most popular pre-hospital analgesic, raising concerns about over-the-counter opioid access during the study period, possible over-prescription in the community or on discharge from hospitals. It is expected that this number should fall in the future due to recent up-scheduling of codeine given its propensity to be overused, thus causing inadvertent harm. There is also the risk that the high use of opioids in the ED inadvertently reinforces its use to treat migraine by patients and GPs in the community. This may be resolved with a migraine action plan, similar to an asthma action plan, reinforcing appropriate medication choices. Such a strategy may also reduce ED attendances for this recurrent illness which can lead to recurrent presentations as we observed.

Despite a large sample size, comparable to similar studies in the field, there are several limitations to our study. As this was a single institution study, generalisability

of results may be limited. Also, comparing prescribing trends to Australian guidelines may limit the applicability of these results on an international level. However, studies from other countries similarly demonstrate opioid over-prescription, suggesting this issue is not limited to Australia. Our retrospective chart analysis methodology limits data collection to what is explicitly documented and physician-associated reasons for varying prescriptions were unable to be captured. Coding errors may have under-estimated the burden of migraine in this ED as a diagnosis of 'headache', for instance, would not have been included in our population. This highlights the need for a prospective study to address this issue. The final diagnosis of migraine may also have been reached after assessment and initial management, thus mitigating the choice to initially prescribe an opioid. However, it highlights the larger issue of opioid over-reliance in the ED setting for undifferentiated headache presentations and when there is a clear past medical history of migraine on presentation. We urge other Australian emergency departments to conduct similar studies to assess migraine treatment patterns and aim to decrease opioid prescriptions.

Our results identify several areas for further research and targeted intervention in acute migraine in order to address the observed polypharmacy and inconsistent prescribing patterns. Factors influencing prescribing patterns, such as differences in prescriptions between junior and senior doctors, require further evaluation in order to design appropriate interventions; this is currently in progress at our institution. We advocate the need for patient-centred education, harm reduction strategies and ED education for front line physicians, and consideration of written handouts for patients before discharge from the hospital.

CONCLUSION:

We observed considerable polypharmacy in ED migraine management with inconsistent prescribing patterns. Recommended medications were infrequently used and opioid use was common. Factors influencing prescribing patterns require further investigation in order to improve rates of guideline recommended treatment.

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Table 1: All medications prescribed for acute migraine in the SVHM ED during study period

Name of medication	Total n/744 (% receiving)
Paracetamol	385 (51.8)
Aspirin	134 (18.0)
Non-steroidal anti-inflammatory drugs (NSAIDs) (excluding aspirin)	Total: 278 (37.4)
- Ibuprofen	247 (33.2)
- Diclofenac	12 (1.6)
- Ketorolac (IV, IM)	10 (1.3)
- Other NSAIDSs†	11 (1.5)
Triptans	Total: 51 (6.9%)
- Sumatriptan (inh, subcut)	49 (6.6)
- Zolmitriptan	1 (0.1)
- Eletriptan	1 (0.1)
Chlorpromazine (PO, IV)	325 (43.7)
Opioids	Total: 345 (46.4)
- Oxycodone immediate release (Endone)	183 (24.6)
- Panadeine forte (paracetamol/codeine 30mg)	88 (11.8)
- Aspalgin (Aspirin/codeine)	74 (10.0)
- Morphine (IV)	34 (4.6)
- Panadeine (paracetamol/codeine 8mg)	29 (3.9)
- Fentanyl (IV)	11 (1.8)
- Tramadol	12 (1.6)
- Other opioids‡	12 (1.6)

Anti-emetics- - Metoclopramide (PO/IV) - Ondansetron (PO/IV) - Prochlorperazine - Tropisetron - Other anti-emetics§	Total: 451 (60.6) 231 (31.0) 90 (12.1) 76 (10.2) 43 (5.8) 3 (0.4)
Steroids (dexamethasone or prednisolone):	18 (2.4)
Benzodiazepines: (diazepam, midazolam, temazepam, oxazepam and clonazepam)	28 (3.8)
Propofol (IV) Ketamine (IV)	3 (0.4) 7 (0.9)
Other prescriptions ¶	21 (2.8)

† Other NSAIDs: celecoxib, naproxen, indomethacin
‡ Other opioids: Codeine phosphate, Oxycodone slow release, Pethidine, Targin (oxycodone + naloxone)
§ Other anti-emetics: Domperidone, Promethazine, Droperidol
¶ Other prescriptions: Dihydroergotamine, Caffeine tablet, Verapamil, Pizotifen, Amlodopine, Amitriptyline, Metoprolol, Magnesium, Gabapentin, Pregabalin, Cetirizine, Ranitidine, Pantoprazole, Pink lady (lignocaine + Mylanta), Baclofen
Abbreviations: inhaled (inh), subcutaneous (subcut), intravenous (IV), intramuscular (IM) and PO (per oral). Unless specified, medications were administered orally.
NB: some used more than one medication.

Supplementary table:

Supplementary Table 1: Analgesia attempted prior to ED presentation

Name of medication:	Total n/744 (%)
Simple analgesia (unspecified)†	11 (1.5)
Paracetamol Paracetamol Osteo	175 (23.5) 4 (0.6)
Aspirin	37 (5.0)
Non- steroidal anti-inflammatory drugs (non-Aspirin) - Ibuprofen - Naproxen - Celecoxib - Other NSAIDs ‡	Total: 131 (17.6) 108 (14.5) 5 (0.7) 2 (0.3) 16 (2.2)
Triptans - Sumatriptan - Rizatriptan - Elatriptan - Other triptan§	Total: 66 (8.9) 35 (4.7) 17 (2.3) 2 (0.3) 12 (1.6)

Dihydroergotamine¶	2 (0.3)
Chlorpromazine (oral)	2 (0.3)
Opioids - Panadeine forte (paracetamol/codeine 30mg) - Oxycodone - Mersyndol - Panadeine (paracetamol/codeine 8mg) - Tramadol - Codeine - Other opioids£	Total: 187 (25.1) 45 (6.1) 42 (5.6) 29 (3.9) 21 (2.8) 20 (2.7) 16 (2.2) 18 (2.4)
Anti-emetics - Metoclopramide - Prochlorperazine - Ondansetron - Promethazine	Total: 47 (6.3) 14 (1.9) 21 (2.8) 7 (0.9) 5 (0.7)
Benzodiazepines- (diazepam, temazepam, alprazolam)	6 (0.8)
Prophylactic agents^	Total: 12 (1.6)
Other prescriptions#	Total: 8 (1.1)

Supplementary Table 1: Abbreviation used:

†no further information documented

‡Non-steroidal anti-inflammatory drugs; Other NSAIDs included: indomethacin, sulindac, diclofenac and unspecified NSAID

§Other triptans: naratriptan, zolmitriptan, unspecified triptan

¶ Dihydroergotamine was discontinued in May 2012 in Australia.

£ Oher opioids: morphine, aspalgin (aspirin + codeine), mersyndol forte, suboxone (buprenorphine + naloxone), pethidine (meperidine)

^Prophylactic agents include: pizotifen, topiramate, verapamil, amitryptiline, sertraline, pregabalin, metoprolol, valproate

Other prescriptions: Hyoscine butylbromide/ Buscopan, migranon (butterbur), pseudoephedrine, prednisolone, anti-histamine (unspecified), caffeine tablet, orphenadrine citrate, 'Spanish analgesic'

NB: some used more than one medication.