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Short Communication

Prescribing for acute migraine in a rural Australian hospital

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Abstract

Introduction: Migraine is an episodic, debilitating form of headache. Guidelines exist for the management of acute migraine, concluding that opioids should be avoided, unless as a last resort. Australian research shows a poor consistency in ED prescribing patterns with no published rural hospital data. Treatment of acute migraine often involves multiple medications used in succession. The overprescription of opioids is reported and often accompanied by an underuse of triptans. Previous studies do not differentiate prescriber intervention over time. It is unclear if opioid medications are routinely selected as first-line therapy in rural Australian EDs. The aim of this research is to complete an evaluation of migraine management in a rural Australian ED and compare trends to pre-existing data.

Methods: This study is a retrospective cohort analysis of clinician-diagnosed migraine patients presenting to a single Australian ED between 1 January 2017 and 31 December 2021. Cases with migraine were defined by a primary G439 diagnosis (International Classification of Diseases 10th Revision). Patients with alternative diagnoses and those who did not wait were excluded. Cases underwent a non-blinded chart review extracting demographic

and clinical data. Diagnoses were not evaluated against the international headache society criteria. ED interventions were recorded as first-, second-, third- or fourth-line based on the ordering time by the prescribing doctor. Medications were classified as being compliant or non-complaint with current standards of care. Trends were compared to previous studies.
Results: A total of 341 patients were diagnosed with migraine, 72.4% female, median 35 years. A total of 6.5% arrived by ambulance, 76.8% had a prior history of migraine, 6.5% were admitted, 36.4% underwent blood investigations and 12.0% neuroimaging. A total of 7.6% of patients received opioids as first-line therapy, 44.3% failed self-medication and 21.7% of patients with migraine history trialled opioids prior to presentation. Regarding prescriptions, 795 were written, 18.1% were non-compliant with guidelines. Seventy percent of patients received dopamine and 5-HT3 antagonists, 43.1% non-steroidal anti-inflammatory drugs (NSAIDs), 27.0% serotonin receptor agonists and 27.0% opioids. There was a statistically significant prescribing difference for aspirin, used in 16.4% of those with a migraine history and 5.1% without (p=0.01). A total of 13.8% reported allergies/contraindications to guideline therapies.
Conclusion: Prescribing for acute migraine in Australia is highly variable by context. This single-site study has similarities and differences with prior research. Rates of opioid prescribing were lower, possibly due to the known sparing effect of serotonin receptor agonist usage. Similar rates of NSAID and intravenous hydration prescription occurred. Patterns of intervention over time in this rural ED demonstrated strong adherence to guidelines and low opioid utilisation. Contextual differences proposed to impact prescribing include staff training, medication availability and shorter wait times. Imaging and pathology investigation rates were lower than in prior research and did not change disposition. Future studies across multiple rural hospitals may help understanding of this topic.

Keywords

acute pain, Australia, emergency services, headache, hospital, migraine disorders.

Introduction

Migraine is an episodic, debilitating form of headache characterised by pain, nausea and aura, causing significant personal morbidity[1]. Evidence is inconclusive whether rurality increases the prevalence or severity of migraines and patients may attend rural EDs for severe symptoms or those refractory to initial analgesia[2-4].

Australian guidelines suggest initial management include aspirin, non-steroidal anti-inflammatory drugs (NSAIDs) or paracetamol, followed by dopamine antagonists and serotonin receptor agonists[5-7]. A consensus view is that opioids should be avoided in the management of migraine unless as a last resort[5-8], and this view is shared by the American Academy of Neurology[9]. Sustained users of opioids risk chronicification of migraine and dependence[8-11].

Recent Australian studies have shown inconsistency in ED prescribing patterns and lack rural hospital data. Guideline compliance is poor and opioids are reportedly overprescribed[12-16], used in almost 50% of presentations to one ED and 23% in another[12,13]. Overuse of opioids is often accompanied by an underuse of triptans[12,14-16].

Treatment of acute migraine often involves multiple medications used in succession. Previous data do not differentiate prescriber intervention patterns over time[12,13].

The aim of this research is to complete a real-world evaluation of migraine management assessing concordance with guidelines, comparing to previously published conclusions and including patients with a known history of migraines. The study assesses patterns of prescriber intervention to hypothesise how rural health barriers and enablers may have impacted prescription decisions in a single rural hospital site.

Methods

This is a retrospective cohort analysis of clinician-diagnosed migraine cases presenting to the Hedland Health Campus ED between 1 January 2017 and 31 December 2021.

This 50-bed centre, with laboratory and CT scanning, serves the Western Australian Pilbara region and is led by staff-grade doctors holding fellowships from the Royal Australian College of General Practitioners or the Australian College of Rural and Remote Medicine. A receiving tertiary centre is a 1619 km journey by fixed-wing retrieval.

Cases with a migraine were defined by a primary G439 International Classification of Diseases (ICD-10) diagnostic code, 'Migraine, unspecified'[17]. The cohort was interrogated, and patients with alternative primary and secondary ICD-10 diagnoses alongside those who did not wait for assessment or left at risk were excluded.

Migraine cases underwent a non-blinded chart review extracting demographic and clinical data. Diagnoses were not evaluated against the International Headache Society criteria as accuracy was not considered within scope for this research or similar recent studies[9,10]. Where a migraine history was undocumented it was assumed absent.

ED interventions and treatment provided were recorded as first-, second-, third- or fourth-line based on the ordering time by the prescribing doctor; no more than four options were prescribed/administered. Medications administered prior to arrival to the ED and nurse-initiated medications were recorded. Follow-up instructions, outpatient prescriptions, consultations, length of stay and disposition outcomes were noted.

De-identified data was analysed using Stata v15.1 (StataCorp; https://www.stata.com). Medications were classified as compliant or non-complaint with current standards of care listed in Appendix I:

- compliant prescribing: presence of medication(s) included in Australian guidelines
- non-compliant prescribing: presence of *any* medication() not included in current Australian guidelines.

Guidelines utilised had high levels of consistency and included those of Therapeutic Guidelines, the Emergency Care Institute, National Prescribing Service, Headache Society of Australia and

Royal Australian College of General Practitioners.

To reduce chart reviewer bias only four health professionals with data collection expertise participated. No conflicts of interest were declared and cases were randomly allocated.

Ethics approval

The project was reviewed by the WA Country Health Service Human Research Ethics Committee and no ethical concerns were raised for publication (reference LNRP 2022.25).

Results

There were 92,216 ED presentations between 1 January 2017 and 31 December 2021, with 348 receiving a primary diagnosis of migraine. Seven were incorrectly coded or did not meet criteria and were excluded. The cohort comprised 270 individuals, some with multiple presentations.

Most cases were female (72.4%) with a median age of 35 years (Table 1). A total of 76.8% reported a prior history of migraine, 6.5% arrived by emergency health service transport (ambulance, medevac); the majority (92.0%) independently self-presented. Blood test investigations were completed in 36.4% of patients, neuroimaging was ordered in 12.0% of presentations. A total of 44.3% (*n*=151) failed self-care medication use prior to ED attendance.

A total of 128 patients with a prior history of migraine trialled medications before presentation. The presence or absence of medication use prior to presentation was recorded in 95.6% of cases; prescribing analysis was completed in the 129 cases where specific medications were documented. Patients who received opioids were less likely to arrive by private transport (odds ratio (OR) 0.17, 95% confidence interval (CI) 0.1–0.3) 0.17 and be older (aged 60–69 years; OR 6.3, 95%CI 3.2–12.4). A total of 60.1% of patients received intravenous fluids.

There were 795 unique medication prescriptions made during the study period (Table 1), with 13.8% of the cohort recounting an allergy or contraindication to non-opioid guideline medications; 18.1% of prescriptions were made for non-guideline medications.

Dopamine and 5-HT3 receptor antagonists were prescribed for 71.0% of patients followed by NSAIDs (excluding aspirin) in 43.1%, opioids and paracetamol (27.0% and 26.7%, respectively) and chlorpromazine for 21.1% of patients. The only statistically significant prescribing difference was aspirin, used in 16.4% of those with a history of migraines and 5.1% without (p=0.01). Similar proportions of patients with and without history of migraine were prescribed opioids, 27.1% and 26.6%, respectively. The only opioid medication considered in the top five options for agents of any line was oxycodone. Ten percent of patients reporting allergy/contraindication to first-line therapy were prescribed opioids.

Multiple pharmaceutical management approaches were used, and frequencies of prescribed medications are shown in Appendix II. Non-guideline medications comprised 18.1% (*n*=144) of all 795 prescriptions.

The most commonly selected options were:

- first-line: ondansetron (13.5% of patients), paracetamol (12.0%), rizatriptan (11.1%), ketorolac (8.5%) and metoclopramide (7.9%)
- second-line: ondansetron (14.4%), rizatriptan (9.4%), ibuprofen (7.9%), paracetamol (7.3%) and ketorolac (6.7%)
- third-line: chlorpromazine (6.4%), paracetamol (6.2%), ondansetron (5.7%), oxycodone (4.7%) and metoclopramide (3.8%)
- fourth-line: rizatriptan (2.6%), promethazine and chlorpromazine (both 2.4%), ibuprofen (2.0%) and prochlorperazine (1.5%).

Table 2 compares the current evidence, including an international comparator[18].

Table 1: Patients receiving any medication class for management of migraine, Hedland Health Campus ED, 1 January 2017 to 31 December 2021 (*N*=341, total number of prescriptions 795)†

Medication class	*n*	%/*p*-value¶
Paracetamol	91	26.69
Aspirin	47	13.78
Non-steroidal anti-inflammatory drugs (excluding aspirin)	147	43.11
Triptans	92	26.98
Chlorpromazine	72	21.11
Opioids	92	26.98
Dopamine and 5-HT3 receptor antagonists (excluding chlorpromazine)	242	70.97
Steroids	1	0.29
Benzodiazepines	4	1.17
Ketamine	2	0.59
Local anaesthetic trigger point injection	1	0.29
Other medications	4	1.17

† Irrespective of order of prescription; patients may have been prescribed more than one medication.

¶ Pearson's χ^2 test *p*-value or Fisher's exact *p*-value (where applicable) is reported.

Table 2: Current body of knowledge regarding ED prescribing for migraine in Australia

Characteristic	Gunasekera, et al (2020)[12]	Joules and Yeoh (2021)[13]	Wijeratne, et al (2022)[18]	Van Bockxmeer, et al (present research)
Research setting	St Vincent's Hospital, Melbourne, Victoria; tertiary 880 beds; 43,000 annual presentations. Specialty-led urban teaching hospital.	Austin Hospital, Melbourne, Victoria; tertiary 840 beds; 90,000 annual presentations. Specialty-led urban teaching hospital, recent migraine quality projects.	Planned substudy of a prospective study in 67 health centres in 10 countries including regional Australia and New Zealand. Australian data not distinguished from whole cohort.	Hedland Health Campus, Port Hedland, Western Australia; rural referral hospital; 50 specialty beds; 27,000 annual presentations. Generalist hospital.
Study period	4 years (2012–2016)	2 years (2019–2020)	One calendar month (March 2019)	4 years (2017–2021)
Number	744 (entire cohort of migraine diagnoses)	75 (random select cohort of migraine diagnoses)	1101 patients	341 (entire cohort of migraine diagnoses)

Prescribing analysis	Presence of opioid medications	Presence of opioid medications	Presence of opioid medications as initial or follow-up (after 30 minutes), by type and administration (self, ambulance, prescriber)	Analysis of pattern of intervention over time
Female (%)	75	76	73.7	72
Median age (years)	36.4	39.0	37	35.0
Pre-hospital medications (%)	64.5	Not reported	49.2	43.4
Pre-hospital opioid (%)	25	13	24	21.7
Arrival by emergency health service (%)	25.0	Not reported	18.1	6.5
Aspirin (%)	18.0	29	10.4	13.8
NSAID (not aspirin) (%)	37.4	37	34.8	43.1
Paracetamol (%)	51.8	55	40.4	26.7
Triptans (%)	6.9	5	4.8	27.0
Chlorpromazine (%)	43.7	51	35.8	21.1
Opioids (total) (%)	46.4	23	24.1	27.0
Opioids (known history of migraine) (%)	45	Not reported	Not reported	27.1
Documented allergies to recommended migraine treatment (%)	17	Not reported	Not reported	14
IV fluid (%)	64.7	Not reported	67.2	60.1
Neuroimaging (%)	17.9	37	31.7 (including MRI)	12.0
Blood tests (%)	64	Not reported	Not reported	36.4
Lumbar puncture (%)	2.8	1	2.1	Not reported
Admission to ward (%)	2.0	Not reported	6.4	5.3
GP referral (%)	33	Not reported	Not reported	30.5
Specialty referral (%)	1	Not reported	Not reported	9.4

NSAID, non-steroidal anti-inflammatory drug.

Discussion

Prescribing patterns for acute migraine are controversial due to concerns surrounding opioid utilisation rates[12,13]. Our single-site evaluation shows that migraine management varies by context[18]. Barriers and enablers impacting prescriber behaviours include health system resourcing, regulatory environments, clinician skills and education, prescribing systems and patient-factors[19]. We will discuss how these may specifically relate to our rural area.

Our radiology and laboratory staff provide an 'on call' service after hours. Neuroimaging rates were half that of urban contexts and, where reported, pathology testing rates also reduced (Table 2). Decreased investigation rates did not affect disposition decision-making and may represent significant differences in rural areas[20].

Local staff training may also be responsible for prescribing differences at our site. Rural medical specialist curricula required our doctors to complete community-based primary care placements[21]. This may increase familiarity with non-IV therapeutic options not typically recommended as first-line by emergency medicine colleges[22]. It is possible this is the reason serotonin receptor agonist usage was four times greater and chlorpromazine less than half in our cohort[12,13].

High accessibility to sublingual serotonin receptor agonists may also have contributed to differences observed. Evidence demonstrates rapid improvement in migraine symptomatology with high rates of serotonin receptor agonist administration known to reduce opioid overuse[12,13,15,16].

Our opioid prescribing rate of 27.0% was significantly lower than the 46.4% reported in an urban Australian site[12]. ED wait times in rural areas are shorter than national averages[23]. Timely assessment may have allowed the successful high early rate of ondansetron prescribing in our cohort, providing quicker symptom control.

When patients received opioids, we attempted to understand factors contributing to this prescription decision. By analysing patterns of intervention over time we affirmed prescriber preservation of opioids as a 'last resort'[5-8]. We found our staff selected opioids as a first-line agent in a minority (7.6%) of patients.

When opioids were used, oxycodone was the most common agent. A total of 13.8% of our cohort recounted an allergy or contraindication to non-opioid guideline medications, therefore opioid prescribing may have been reasonable for some patients receiving them. This is not consistent with a previously reported over-reliance on this mediation class in Australian EDs. Further exploration of our hypothesised reasons is needed[12].

This project gives insight into prescribing practices by rural generalists at an Australian site. There are limitations to our conclusions. Data collectors were not blinded to the outcome of the cohort study. Direct comparison to previous research was not available and other sites were not involved. Medication selection and availability may not be comparable to all Australian EDs. The prescribing guidelines themselves were not challenged, and the authors acknowledge this could create potential inconsistencies with some providers considering the use of droperidol or ketamine

for acute migraine[24]. This study is retrospective in nature, so current and previous diagnoses of migraines were not confirmed and the impact of co-diagnoses was not evaluated.

Conclusion

We conclude that real-world prescribing varies highly by individual practice context. Patterns of intervention over time in our rural ED demonstrated strong guideline adherence and low opioid utilisation rates.

Other prescribing barriers and enablers unique to this context include differences in staff training, medication availability and shorter wait times. We hypothesise these were responsible for greater utilisation of opioid-sparing serotonin receptor agonist therapy and rapid symptom control through early ondansetron administration.

Imaging and pathology investigation rates were significantly lower and did not change disposition. A future prospective study to analyse prescriber intent across multiple rural sites may help further understanding of this topic and development of context-specific practice resources.

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Conflicts of interest

The authors declare no conflicts of interest.

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Appendix I: Australian Migraine Treatment Guideline medications

Guideline	Web page
Emergency Care Institute	https://aci.health.nsw.gov.au/networks/eci/clinical/clinical-tools/neurology/headache/migraine
NPS MedicineWise	https://www.nps.org.au/australian-prescriber/articles/migraine-management
Migraine & Headache Australia	https://headacheaustralia.org.au/migraine/acute-medications
Therapeutic Guidelines	https://www.tg.org.au
Royal Australian College of General Practitioners	https://www.racgp.org.au/afpbackissues/2005/200508/200508joubert2.pdf

Class	Medication	Guidelines
Paracetamol	Paracetamol	ETG, NPS, HSA, RACGP
Aspirin	Aspirin	ETG, NPS, HSA, RACGP
Non-steroidal anti-inflammatory drugs	Ibuprofen	ETG, NPS, HSA, RACGP
	Ketorolac	ETG, NPS, HSA
	Other/COX2	ETG, NPS
Serotonin receptor agonists	Sumatriptan	ETG, NPS, HSA, RACGP
	Zolmitriptan	ETG, NPS, HSA, RACGP
	Eletriptan	ETG, NPS, HSA, RACGP
Opioids	All agents	N
Dopamine antagonists	Metoclopramide	ETG, NPS, HSA, RACGP
	Domperidone	ETG, NPS, HSA, RACGP
	Prochlorperazine	ETG, NPS, HSA, RACGP
	Chlorpromazine	ETG, NPS, RACGP
5-HT3 receptor antagonists	Ondansetron	ETG, NPS
Butyrophenone	Droperidol	N
Corticosteroids	Prednisolone	ETG
	Dexamethasone	N
Benzodiazepines	All agents	N
Non-barbiturate sedatives	Propofol	N
Dissociative anaesthetics	Ketamine	N
Ergot alkaloids	Ergotamine	ETG, NPS, HSA, RACGP

ETG, Therapeutic Guidelines. HSA, N, no relevant guidelines. NPS, NPS MedicineWise.

Appendix II: Frequency of prescribed medications by prescriber pattern of intervention over time, 2017–2021 (*N*=341)

Class/action	Prescribed medication	First-line		Second-line		Third-line		Fourth-line		Guideline	OTC
		n	%	*n*	%	*n*	%	*n*	%		
Paracetamol	Paracetamol	41	12.02	25	7.33	21	6.16	4	1.17	ETG, NPS, HSA, RACGP	Yes
Aspirin	Aspirin	20	5.87	19	5.57	4	1.17	4	1.17	ETG, NPS, HSA, RACGP	Yes
NSAIDs (excluding aspirin)	Ibuprofen	21	6.16	27	7.92	11	3.23	7	2.05	ETG, NPS, HSA, RACGP	Yes
	Ketorolac	29	8.50	23	6.74	5	1.47	1	0.29	ETG, NPS, HSA	No
	Paracoxib	7	2.05	9	2.64	5	1.47	1	0.29	N	Yes
	Celecoxib					1	0.29			N	
Serotonin receptor agonists	Sumatriptan	1	0.29							ETG, NPS, HSA, RACGP	No
	Rizatriptan	38	11.14	32	9.38	12	3.52	9	2.64	ETG, NPS, HSA, RACGP	
Chlorpromazine	Chlorpromazine	22	6.45	20	5.87	22	6.45	8	2.35	ETG, NPS, RACGP	No
Opioids	Oxycodone	15	4.40	20	5.87	16	4.69	4	1.17	N	No
	Paracetamol/codeine	2	0.59	2	0.59	1	0.29	1	0.29	N	No
	Morphine	3	0.88	2	0.59	1	0.29	1	0.29	N	No
	Fentanyl	1	0.29	4	1.17	1	0.29	3	0.88	N	No
	Tramadol	5	1.47	4	1.17	5	1.47	1	0.29	N	No
Dopamine and 5-HT3 receptor antagonists, excluding chlorpromazine	Metoclopramide	27	7.92	21	6.16	13	3.81	1	0.29	ETG, NPS, HSA, RACGP	Yes/No
	Ondansetron	46	13.49	49	14.37	19	5.57	1	0.29	ETG, NPS	No
	Prochlorperazine	26	7.62	6	1.76	6	1.76	5	1.47	ETG, NPS, HSA, RACGP	No
	Droperidol	5	1.47					1	0.29	N	No
	Promethazine	4	1.17	2	0.59	2	0.59	8	2.35	N	
Corticosteroids	Dexamethasone					1	0.29			N	No
Benzodiazepines	Diazepam			3	0.88	1	0.29			N	No
Dissociative anaesthetic agents	Ketamine					1	0.29	1	0.29	N	No
Local anaesthetic trigger point injection	Bilateral cervical bupivacaine injection			1	0.29					N/A	
Other chronic migraine medications	Pizotifen†	1	0.29							N/A	No
	Lamotrigine					1	0.29	1	0.29	N/A	No
	Propranolol†			1	0.29					N/A	No

†Regular migraine medications, not used in the acute treatment setting.

ETG, Therapeutic Guidelines. HSA, Migraine & Headache Society of Australia. N, no relevant guidelines. N/A, not available. NPS, NPS MedicineWise. NSAID, non-steroidal anti-inflammatory drug. OTC, over the counter. RACGP, Royal Australian College of General Practitioners.

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