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CONTROVERSIE IN NEUROLOGIA D'EMERGENZA E URGENZA

29 SETTEMBRE
1 OTTOBRE 2022

ROMA

"Sapienza" University of Rome

Polo Pontino

erapia delle cefalee primarie in PS?

Triptani NO

Cherubino Di Lorenzo

Dipartimento di Scienze e Biotecnologie medico-chirurgiche

Headache

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Review Article

Management of Adults With Acute Migraine in the Emergency Department: The American Headache Society Evidence Assessment of Parenteral Pharmacotherapies

Serena L. Orr, MD; Benjamin W. Friedman, MD, MS; Suzanne Christie, MD, FRCPC; Mia T. Minen, MD; Cynthia Bamford, MD; Nancy E. Kelley, MD, PhD; Deborah Tepper, MD

Recommendation for Acute Management of Migraine	Medication
Must offer (level A)	None
Should offer (level B)	Metoclopramide IV
	Prochlorperazine IV
	Sumatriptan SC
May offer and may avoid (level C)	Acetaminophen IV
	Acetylsalicylic acid IV
	Chlorpromazine IV
	Dexketoprofen IV
	Diclofenac IM
	Dipyrone IV
	Droperidol IM
	Haloperidol IV
	Ketorolac IV/IM
	Valproate/valproic acid IV
Avoid	Diphenhydramine IV
	Hydromorphone IV
	Lidocaine IV
	Morphine IV
	Octreotide IV
No recommendation (level U)	Dexamethasone IV
	Dihydroergotamine IV/SC
	Ergotamine SC
	Ketamine IV
	Lysine clonixinate IV
	Magnesium IV
	Meperidine IM
	Nalbuphine IV
	Propofol IV
	Promethazine IV
	Tramadol IM
	Trimethobenzamide IM
Prevention of migraine recurrence should offer	Dexamethasone IV

IM = intramuscular; IV = intravenous; SC = subcutaneous.

Internal and Emergency Medicine (2020) 15:109–117
https://doi.org/10.1007/s11739-019-02266-2

EM - REVIEW

Acute headache management in emergency department. A narrative review

Maria Adele Giamberardino[1] · Giannapia Affaitati[1] · Raffaele Costantini[2] · Martina Guglielmetti[3,4] · Paolo Martelletti[4,5]

Table 6 Main options for acute treatment of primary headaches in the ED

NSAIDs (Migraine and TTH)
Ketorolac (60 mg IM, 30 mg or 60 mg IV)
Diclofenac (75 mg IM)
Triptans (Migraine and CH)
Sumatriptan (6 mg SC)
Neuroleptic Antiemetics/Dopaminergic antagonists (All forms)
Chlorpromazine (25–50 mg IV)
Prochlorperazine (10 mg IV)
Metoclopramide (10 mg IV)
Opioids (Severe, refractory headaches only)
Morphine (5–10 mg IM, 2–5 mg IV)
Steroids (Migraine, Status Migrainosus, CH)
Dexamethasone (4–10 mg IV, followed by 4 mg every 6 h if necessary)
Oxygen (CH)
7 l/min for 10–15 min with a mask

ED Emergency Department, *NSAIDs* Non Steroidal Antiinflammatory Drugs, *TTH* Tension-type headache, *CH* Cluster headache, *IM* intramuscularly, *IV* intravenously

Received: 6 April 2021 | Accepted: 23 July 2021
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RESEARCH SUBMISSIONS

Epidemiology, investigation, management, and outcome of headache in emergency departments (HEAD study)—A multinational observational study

Some patients (35.5%, 95% CI: 34.1%–36.9%) had taken medication before attending the ED.

TABLE 4 Emergency department (ED) diagnosis

ED diagnosis (total sample 4536)	Number, %	Percent (95% CI)
Presumed primary nonmigraine headache (not otherwise classified)	1598, 35.2%	33.9%–36.6%
Migraine	1101, 24.3%	23.0%–25.5%
Tension-type headache	317, 7.0%	6.3%–7.8%

Initial treatment—within 30 min of medical assessment (total sample 4536)					
Any medication given	3449, 76.0% (74.8%–77.3%)				Missing data
Note: More than one medication is possible	Total (N, %, 95% CI)	95% CI	Oral	Parenteral (IM/IV)	1
Paracetamol	1575, 34.7%	33.4%–36.1%	1275	300	
Aspirin	141, 3.1%	2.6%–3.7%	140	1	
NSAID (non-aspirin)	1367, 30.1%	28.8%–31.5%	634	733	
Any opioid	832, 18.3%	17.3%–19.5%			
Codeine-containing medication	298, 6.6%	5.9%–7.3%	285	14	
Oxycodone	231, 5.1%	4.5%–5.8%	228	3	
Pethidine/meperidine	8, 0.2%	0.09%–0.4%	2	6	
Other opioid	295, 6.5%	5.8%–7.3%	101	194	
Triptan	48, 1.0%	0.8%–1.4%	32	16	
Chlorpromazine	145, 3.2%	2.7%–3.8%	11	134	
Prochlorperazine	282, 6.2%	5.6%–7%	66	216	
Droperidol/haloperidol	22, 0.5%	0.3%–0.7%	6	16	
Metoclopramide	451, 9.9%	9.1%–10.8%	101	350	
Ondansetron	412, 9.1%	8.3%–10%	281	131	
Ergots	5, 0.1%	0.05%–0.3%	5	0	
Corticosteroid	38, 0.8%	0.06–1.1%	12	26	
Antibiotic/antiviral agent	62, 1.4%	1%–1.8%	19	43	
Other treatments					
Oxygen	54, 1.2%	0.09%–1.6%			
Acupuncture	1, 0.02%	0%–0.1%			
IV fluids	548, 12.1%	11.2%–13.1%			

Note: 95% CI were estimated using http://vassarstats.net/prop1.html Method Wilson, no continuity correction.

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DOI: 10.1111/head.14293

RESEARCH SUBMISSIONS

Current practice for primary headache disorders and perspectives on peripheral nerve blocks among emergency physicians in Canada: A national survey

Dilan Patel MSc[1,2] | Monica Taljaard PhD[1,2] | Krishan Yadav MD, MSc[2,4] | Daniel James MD[3,4] | Jeffrey J. Perry MD, MSc[1,2,4]

CONCLUSIONS

Using iv NSAIDs alone, as well as dopamine receptor antagonists with or without ketorolac are commonly used pharmacotherapies for primary headache disorders in Canadian EDs. Importantly, a large proportion of physicians have never used a PNB in their practice. Among those who have experience with PNBs, the majority find them safe and effective. The vast majority of respondents would consider PNBs as a first-line treatment option given sufficient evidence from a future trial.

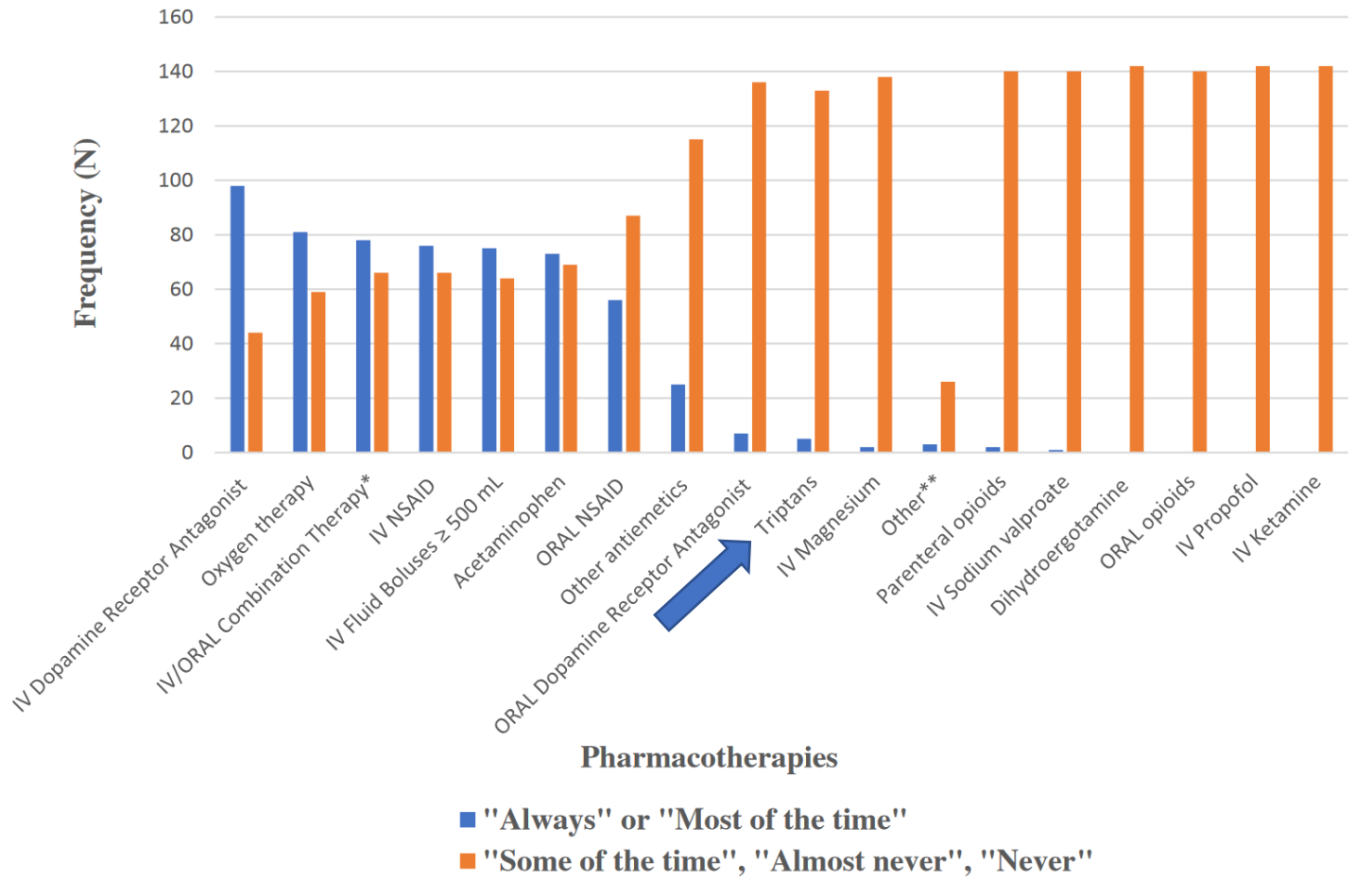

FIGURE 2 Current routine practice for primary headaches—frequency of use of pharmacotherapies ($N = 144$). *IV or ORAL co-administration of ketorolac and a dopamine receptor antagonist. **Other: dexamethasone was most frequently reported. NSAIDs, nonsteroidal anti-inflammatory drugs [Color figure can be viewed at wileyonlinelibrary.com]

Journal of
Clinical Medicine

MDPI

Article

Trends in the Management of Headache Disorders in US Emergency Departments: Analysis of 2007–2018 National Hospital Ambulatory Medical Care Survey Data

Weighted Visits	All Headaches	Migraine	NOS Headaches	
	10.2 Million (100.0%)	3.4 Million (32.9%)	6.6 Million (63.9%)	
Characteristics	Weighted %	Weighted %	Weighted %	SMD [a]
No. of medications administered in ED				0.50
0	21.3	12.3	26.4	
1	10.5	5.2	13.3	
2	14.8	14.9	14.2	
≥3	53.5	67.6	46.1	
No. of medications prescribed at discharge				0.16
0	54.1	60.7	50.4	
1	21.1	17.2	22.7	
2	15.3	15.4	15.6	
≥3	9.5	6.6	11.3	

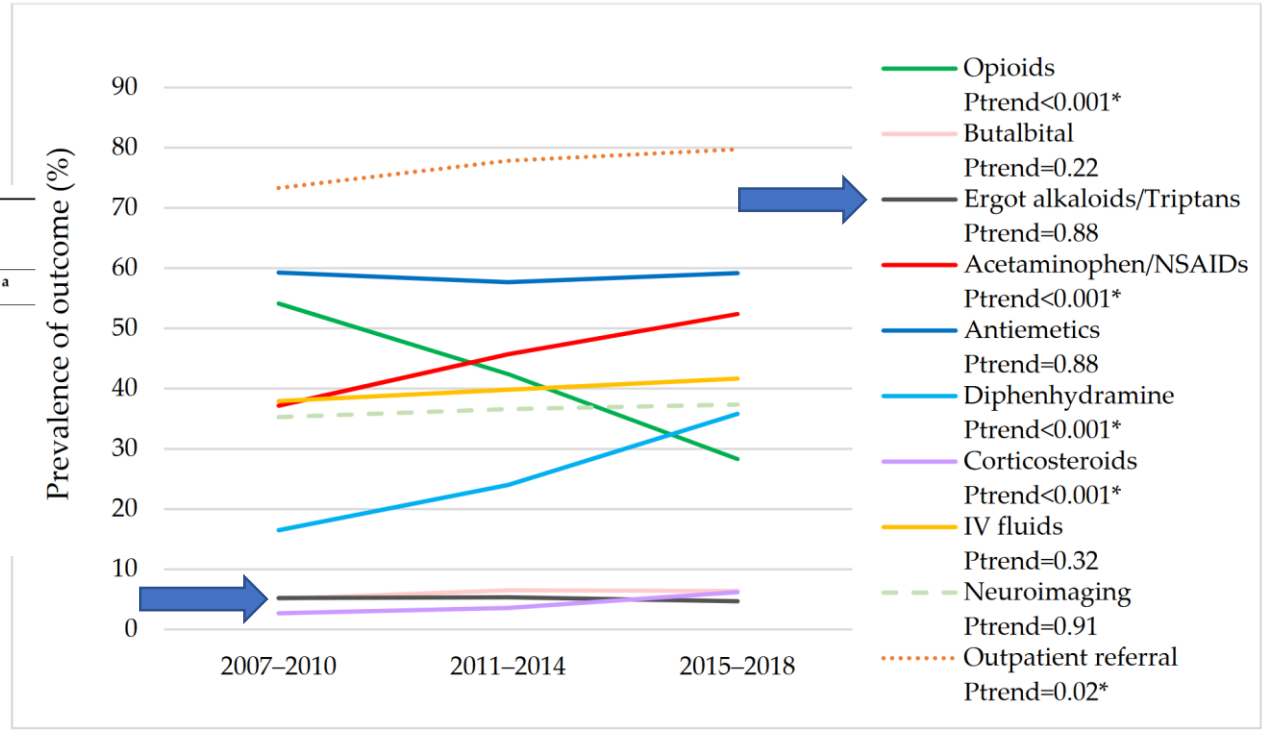

Figure 1. Trends in medication use, neuroimaging use, and referrals to follow-up among headache-related ED visits: 2007 to 2018 NHAMCS data. Abbreviations: ED: Emergency Department; NHAMCS: National Hospital Ambulatory Medical Care Survey; NSAIDs: nonsteroidal anti-inflammatory drugs; IV: intravenous. * A statistically significant trend with $P_{trend} < 0.001$. All P_{trend} were adjusted for age, sex, race, payment source, and practice region.

Internal and Emergency Medicine (2021) 16:2243–2249
https://doi.org/10.1007/s11739-021-02698-9

EM - ORIGINAL

Acute migraine management in the emergency department: experience from a large Spanish tertiary hospital

María Pilar Navarro-Pérez[1,2] · Sara Ballesta-Martínez[1] · Joana Rodríguez-Montolio[1] · Elena Bellosta-Diago[1,2] · José Alberto García-Noaín[3] · Sonia Santos-Lasaosa[1,2]

Table 3 Drugs administered in the Emergency Department ($n=654$)

Medication name	n (%)
NSAIDs	530 (81%)
Triptans	7 (1.1%)
Paracetamol	122 (18.7%)
Metamizole	255 (39%)
Opioids	84 (12.8%)
Benzodiazepines	125 (19.1%)
Antiemetics	282 (43.1%)
Corticoids	144 (22%)
IV fluids	106 (16.2%)
Neuroleptics	1 (0.2%)
Valproate acid	3 (0.5%)

NSAIDs, non-steroidal-anti-inflammatory drugs; IV, Intravenous

Acute migraine treatment prior to the ED visit ($n=528$; 62.3%)	
Triptans	261 (49.5%)
NSAIDs	300 (56.9%)
Metamizole	120 (22.8%)
Paracetamol	98 (18.6%)
Opioids	19 (3.6%)
Antiemetics	19 (3.6%)
Others	27 (5.1%)

Table 5 Acute and prophylactic migraine medications prescribed at ED discharge

Prophylactic migraine treatment $n=69$		Acute migraine treatment $n=516$	
Medication	n (%)	Medication	n (%)
Topiramate	13 (18.8%)	Triptans	129 (25.0%)
Betablockers	14 (20.3%)	NSAIDs	432 (83.7%)
Amitriptyline	24 (34.8%)	Metamizole	142 (27.5%)
Flunarizine	12 (17.4%)	Paracetamol	78 (15.1%)
Neuromodulators	3 (4.3%)	Antiemetics	75 (14.5%)
Antidepressants	1 (1.4%)	Benzodiazepines	44 (8.5%)
Others	3 (4.3%)	Opioids	26 (5.0%)

ED, Emergency Department; NSAIDs, non-steroidal-anti-inflammatory drugs


American guidelines
Italian guidelines
It's always been done this way

Medication, Dose, Route of Administration	Summary of Evidence	Conclusion About Efficacy	Adverse Medication Effects	Principles of Medication Action	Recommendation
Sumatriptan 6 mg SC	Class 1: Comparable to metoclopramide (n = 78) No difference between trimethobenzamide but inadequately powered (n = 40) Inferior to prochlorperazine (n = 66) Superior to placebo (n = 158) Superior to placebo (n = 639) Superior to placebo (n = 51) Superior to placebo (n = 577) Class 2: Superior to placebo (n = 1104) Superior to placebo and acetylsalicylic acid (n = 275) Superior to placebo (n = 277) Superior to placebo (n = 86) Superior to placebo (n = 76) Superior to placebo (n = 242) Inferior to propofol (n = 90) Superior to placebo (n = 235) Superior to placebo (n = 266) Class 3: Superior to placebo (n = 136) Superior to placebo (n = 200) Superior to placebo (n = 209) Superior to placebo (n = 170) Superior to placebo (n = 138) Inferior to metoclopramide (n = 124) Mixed outcomes vs DHE (n = 310)	Highly likely to be effective	In ED-based studies, adverse events in 50% of patients	Most effective if administered very early after migraine onset	Should offer

To relieve the acute headache, subcutaneous **sumatriptan** should be offered to adults who present to an ED with acute migraine (Should offer–Level B). In the ED, sumatriptan may be less efficacious than intravenous anti-dopaminergics. Sumatriptan is not appropriate for patients with contra-indications to this medication and should not be offered to those who have used ergotamine, DHE, or a triptan medication within the previous 24 hours. Unpleasant side effects have occurred in 50% of ED patients administered this medication (Table 2),[54] though irreversible adverse events in patients with low cardiovascular risk are exceedingly uncommon.

Headache

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Review Article

Management of Adults With Acute Migraine in the Emergency Department: The American Headache Society Evidence Assessment of Parenteral Pharmacotherapies

Serena L. Orr, MD; Benjamin W. Friedman, MD, MS; Suzanne Christie, MD, FRCPC; Mia T. Minen, MD; Cynthia Bamford, MD; Nancy E. Kelley, MD, PhD; Deborah Tepper, MD

Efficacy and safety of intravenous acetylsalicylic acid lysinate compared to subcutaneous sumatriptan and parenteral placebo in the acute treatment of migraine. A double-blind, double-dummy, randomized, multicenter, parallel group study

HC Diener for the ASASUMAMIG Study Group*

Cephalalgia

Diener HC for the ASASUMAMIG Study Group. Efficacy and safety of intravenous acetylsalicylic acid lysinate compared to subcutaneous sumatriptan and parenteral placebo in the acute treatment of migraine. A double-blind, double-dummy, randomized, multicenter, parallel group study. Cephalalgia 1999;19:581–8. Oslo. ISSN 0333-1024

Two-hundred-and-seventy-eight patients with acute migraine attacks with or without aura were treated in 17 centers with 1.8 g lysine acetylsalicylate i.v. (Aspisol®; =1 g acetylsalicylic acid), 6 mg sumatriptan s.c. or placebo using a double-blind, double-dummy, randomized, multicenter parallel group study design. Two-hundred-and-seventy-five of them fulfilled the criteria for efficacy analysis, corresponding to 119 patients treated with lysine acetylsalicylate (L-ASA), 114 with sumatriptan and 42 with placebo injections. Both treatments were highly effective compared to placebo ($p < 0.0001$) in decreasing headache from severe or moderate to mild or none (verbal rating scale, VRS, placebo = 23.8%). Sumatriptan showed a significantly ($p = 0.001$) better response (91.2%) compared to L-ASA (response 73.9%). Of the patients in the L-ASA-group, 43.7% were pain-free after 2 h; 76.3% after sumatriptan and 14.3% after placebo. It took patients on average 12.6 (L-ASA), 8.2 (sumatriptan), and 19.4 h (placebo) to be able to work again. There was no significant difference between treatment groups in recurrence of headache in responders within 24 h (18.2% L-ASA, 23.1% sumatriptan, 20% placebo). Accompanying symptoms (nausea, vomiting, photophobia, phonophobia, and visual disturbances) improved with both verum treatments to a similar extent. L-ASA was significantly better tolerated than sumatriptan (adverse events L-ASA 7.6%, sumatriptan 37.8%). In conclusion, subcutaneous sumatriptan and lysine acetylsalicylate i.v. are effective treatments for patients suffering from migraine attacks. Sumatriptan is more effective, but resulted in more adverse events. □

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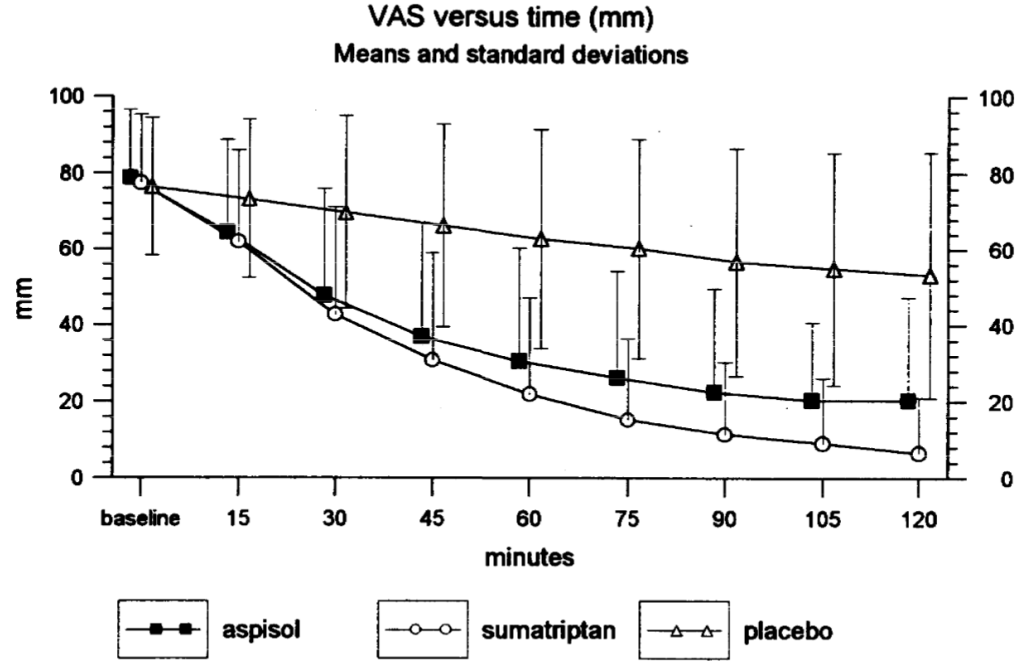

Fig. 2. Change of pain intensity measured by visual analog scale at baseline and up to 120 min after treatment with acetylsalicylic acid, sumatriptan, or placebo.

Table 3. Efficacy parameters.

	L-ASA		Sumatriptan		Placebo		Statistical analysis	
	$n=119$	%	$n=114$	%	$n=42$	%	p_2	p_3
Primary efficacy parameter								
VRS-response 3/2 to 1/0	88	73.9	104	91.2	10	23.8	0.001	<0.0001
Secondary efficacy parameters								
VAS-response responder	90	75.6	108	94.7	12	28.6	<0.0001	<0.0001
Pain free after 2 h	52	43.7	87	76.3	6	14.3	<0.0001	<0.0001
Recurrence of headache within 24 h	16	18.2	24	23.1	2	20.0	0.4	0.7
Need of rescue medication	5	4.2	2	1.8	7	16.7	0.4	0.001

p_2 result of comparison of treatment groups 1, 2.
p_3 result of comparison of all treatment groups.

Table 7. Patients with adverse events.

	L-ASA		Sumatriptan		Placebo		Test results	
Patients affected by	$n=119$	%	$n=116$	%	$n=43$	%	p_2	p_3
Adverse events	9	7.6	38	32.8	4	9.3	<0.0001	<0.0001
Adverse event probably related to test drug	2	1.7	17	14.7	1	2.3	<0.0001	<0.0001

p_2 test result of comparison of treatment groups 1, 2.
p_3 test result of comparison of all treatment groups.

International Emergency Nursing 27 (2016) 51–55

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journal homepage: www.elsevier.com/locate/aaen

Systematic review: Is Metoclopramide more effective than Sumatriptan in relieving pain from migraine in adults in the Emergency Department (ED) setting?

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ABSTRACT

Migraine headache is a common disorder; patients attending Emergency Departments (ED) for migraine symptoms internationally account for 1–3% of total ED annual attendances.

A systematic review was undertaken of reports comparing the effectiveness of metoclopramide intravenously (IV) with that of sumatriptan subcutaneously (SC), in an ED setting, for the immediate relief of migraine and their measurable effects in relieving pain intensity.

Findings of two identified comparable reports confirm the individual efficacy of the study drugs in pain relief. However, whilst one report concludes that there is no statistical or significant clinical advantage for one drug over the other, the other report suggests that metoclopramide has a distinct advantage.

One study is well structured methodologically, but the other has significant risk of bias.

The analysis of the chosen studies demonstrates the need for rigorous study design and robust reporting requirements to obviate this risk. Further studies are required to explore comparable effect.

Implications for clinical practice from the report outcomes indicate the individual effectiveness of both study drugs in providing pain relief for migraine in the Emergency setting, but not the comparable efficacy of one drug over the other.

Risk of bias.

Risk of bias domain	Friedman et al. (2005)	Talabi et al. (2013)	Potential areas of bias
Selection	+	–	Random sequence, allocation concealment
Performance	+	–	Blinding of participants and staff
Detection	+	–	Blinding of specified outcome assessment
Attrition	+	+	Incomplete outcome data, intention to treat
Reporting	+	–	Completeness as per method statement
Other	+	–	Selective reporting of other studies

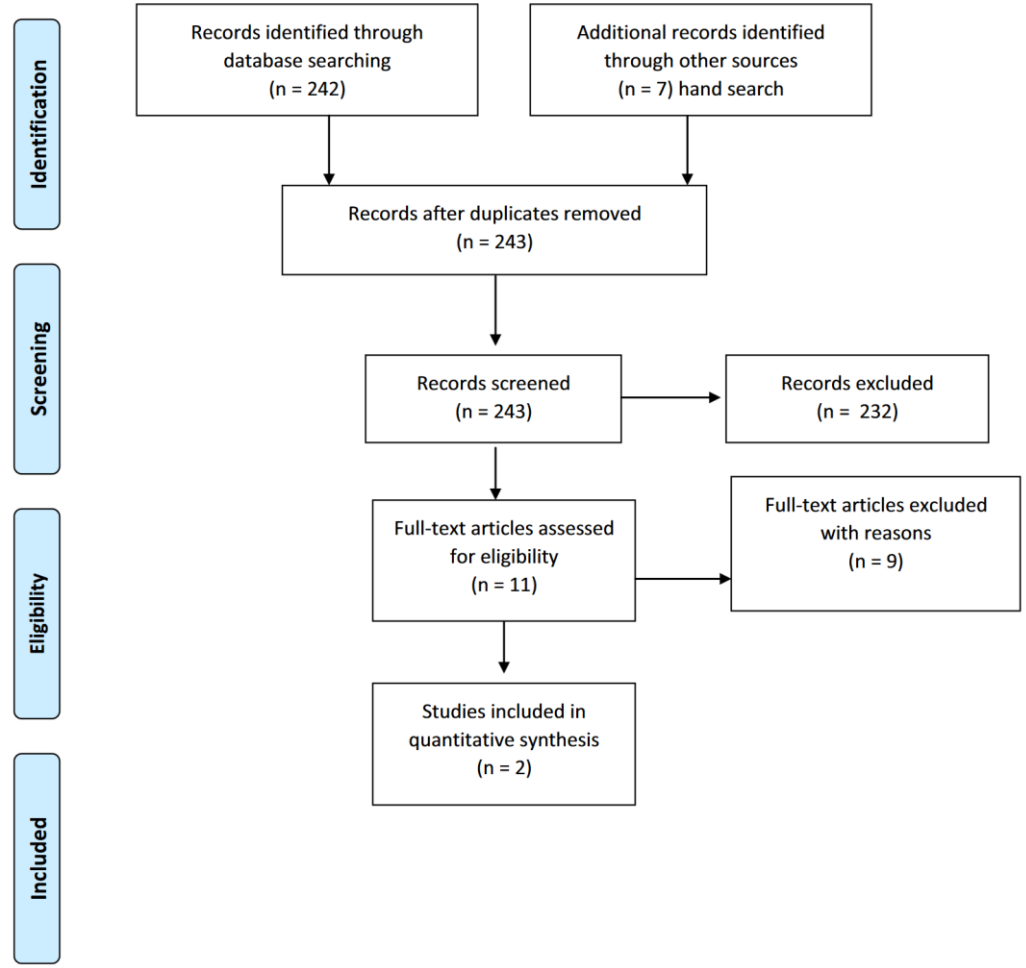

Fig. 1. PRISMA flow diagram (Moher et al., 2009).

Both studies point to significant pain reduction achieved by both drugs in line with other studies. Friedman et al. (2005) indicate a non-significant advantage for either drug at the primary endpoint of 2 hours, whilst Talabi et al. (2013) suggest metoclopramide has a greater effect at the primary end point of 1 hour. The outcomes of these comparative studies confirm the individual efficacy of the study drugs, but they do not agree about the efficacy of one over the other. However, as highlighted above, Talabi et al.'s (2013) study shows methodological flaws and significant risk of bias.

Global Health & Medicine. 2020; 2(4):259-262.

COMMUNICATION

DOI: 10.35772/ghm.2020.01011

Metoclopramide versus sumatriptan in the treatment of migraine in the emergency department: a single-center, open-label, cluster-randomized controlled non-inferiority trial

Yumi Funato[1,*], Akio Kimura[1], Wataru Matsuda[1], Tatsuki Uemura[1], Kentaro Fukano[2], Kentaro Kobayashi[1], Ryo Sasaki[1]

[1] Department of Emergency Medicine and Critical Care, Center Hospital of the National Center for Global Health and Medicine, Tokyo, Japan;
[2] Department of Anesthesiology and Critical Care Medicine, Saitama Medical Center, Jichi Medical University, Saitama, Japan.

Abstract: Migraine is a common disease seen in the emergency department (ED). Triptans, which are recommended in therapeutic guidelines for migraine, have some contraindications and possible severe side effects. Metoclopramide, which is commonly used as an antiemetic, also seems to have pain-relieving effects for migraine. In this article, we will introduce a study in progress, which investigates whether metoclopramide 10 mg intravenously (IV) is non-inferior to sumatriptan 3 mg subcutaneously (SQ) as migraine treatment in the ED. This study is a single-center, open-label, cluster-randomized controlled trial of 80 patients with migraine attacks to investigate the non-inferiority of metoclopramide to sumatriptan. The patients will be cluster-randomized monthly into metoclopramide 10 mg IV and sumatriptan 3 mg SQ arms. The primary outcome will be change in Numerical Rating Scale score for headache at 1 h after baseline. In discussion, if our hypothesis is confirmed, metoclopramide can be considered as first-line medication for migraine attacks in ED settings.

Keywords: study protocol, emergency department, pain management, primary headache

[Intervention Review]

Paracetamol (acetaminophen) with or without an antiemetic for acute migraine headaches in adults

Sheena Derry[1], R Andrew Moore[2]

[1]Oxford, UK. [2]Plymouth, UK

Authors' conclusions

Paracetamol 1000 mg alone is statistically superior to placebo in the treatment of acute migraine, but the NNT of 12 for pain-free response at two hours is inferior to at of other commonly used analgesics. Given the low cost and wide availability of paracetamol, it may be a useful first choice drug for acute migraine in those with contraindications to, or who cannot tolerate, non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin. The addition of 10 mg metoclopramide gives short-term efficacy equivalent to oral sumatriptan 100 mg. Adverse events with paracetamol did not differ from placebo; serious and/or severe adverse events were slightly more common with sumatriptan than with paracetamol plus metoclopramide.

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DOI: 10.1111/head.14307

RESEARCH SUBMISSION

A randomized trial of ketorolac and metoclopramide for migraine in the emergency department

Lawrence P. Richer MD, MSc[1,2] | Samina Ali MD[1,2,3] | David W. Johnson MD[4] | Rhonda J. Rosychuk PhD[1,2] | Amanda S. Newton PhD[1,2] | Brian H. Rowe MD, MSc[2,3,5]

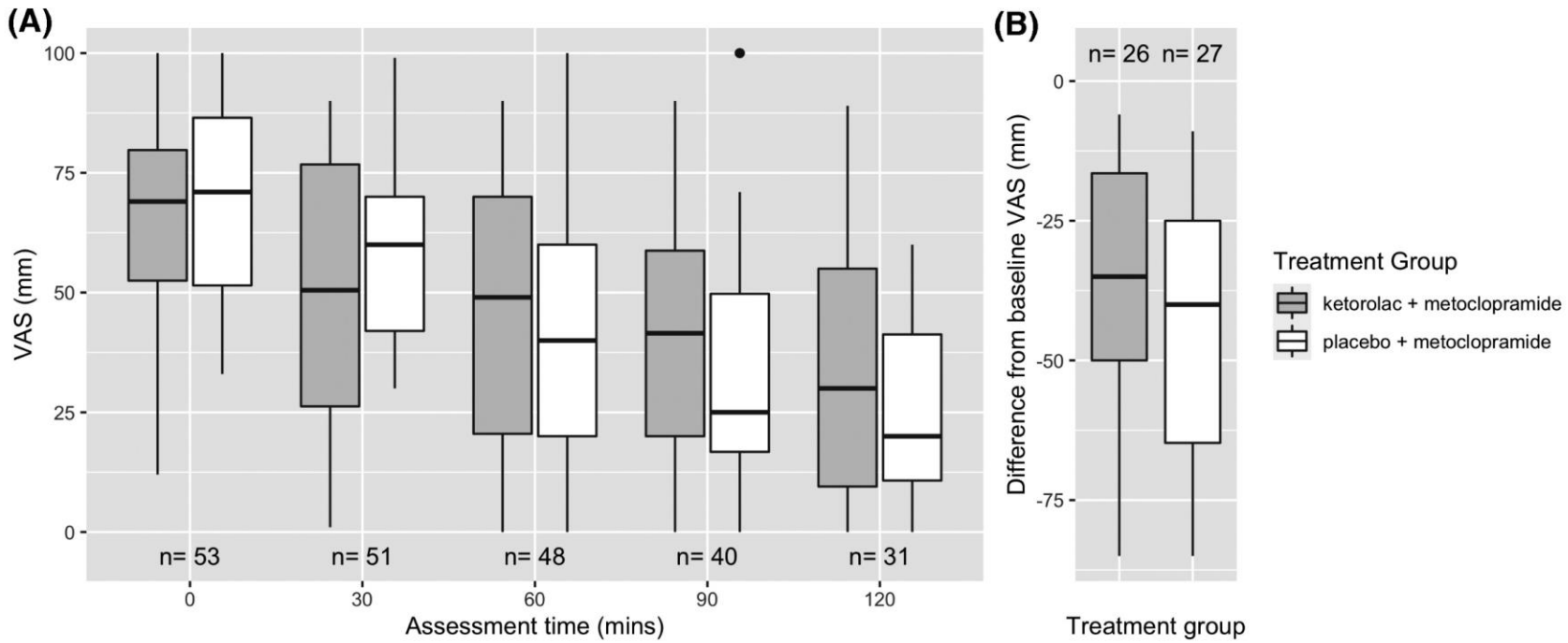

FIGURE 2 (A) Box plot of VAS (mm) by treatment group at baseline, 30, 60, 90, and 120. (B) Overall mean decrease from baseline on VAS divided by treatment group without the last value caried forward for participants who left the ED earlier. ED, emergency department; VAS, Visual Analog Scale

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https://doi.org/10.1007/s11739-019-02266-2

EM - REVIEW

Acute headache management in emergency department. A narrative review

Maria Adele Giamberardino[1] · Giannapia Affaitati[1] · Raffaele Costantini[2] · Martina Guglielmetti[3,4] · Paolo Martelletti[4,5]

If not contraindicated, due to the vasoconstrictive effect (they should be avoided in patients with uncontrolled hypertension, coronary artery disease, or in patients with basilar or hemiplegic migraine) subcutaneous sumatriptan is reported to be effective in 87% of migraine attacks and able to abort the majority of cluster headache attacks.

Sumatriptan should not be administered to patients with headache and associated neurologic deficits, especially considering that it is often difficult to differentiate, in the ED, a migraine with aura from an evolving ictus. It should thus be administered only to patients where a definite diagnosis has been ascertained and not be used as a diagnostic test, also considering that headache forms associated with meningitis and giant arteritis can respond to it

Table 6 Main options for acute treatment of primary headaches in the ED

NSAIDs (Migraine and TTH)
Ketorolac (60 mg IM, 30 mg or 60 mg IV)
Diclofenac (75 mg IM)
Triptans (Migraine and CH)
Sumatriptan (6 mg SC)
Neuroleptic Antiemetics/Dopaminergic antagonists (All forms)
Chlorpromazine (25–50 mg IV)
Prochlorperazine (10 mg IV)
Metoclopramide (10 mg IV)
Opioids (Severe, refractory headaches only)
Morphine (5–10 mg IM, 2–5 mg IV)
Steroids (Migraine, Status Migrainosus, CH)
Dexamethasone (4–10 mg IV, followed by 4 mg every 6 h if necessary)
Oxygen (CH)
7 l/min for 10–15 min with a mask

ED Emergency Department, *NSAIDs* Non Steroidal Antiinflammatory Drugs, *TTH* Tension-type headache, *CH* Cluster headache, *IM* intramuscularly, *IV* intravenously

Efficacy of a Fixed Combination of Indomethacin, Prochlorperazine, and Caffeine Versus Sumatriptan in Acute Treatment of Multiple Migraine Attacks: A Multicenter, Randomized, Crossover Trial

Vincenzo Di Monda, MD; Maria Nicolodi, MD; Antonina Aloisio, MD; Pierluigi Del Bianco, MD; Marco Fonzari, MD; Irene Grazioli, MD; Carla Uslenghi; Leonardo Vecchiet, MD; Federigo Sicuteri, MD

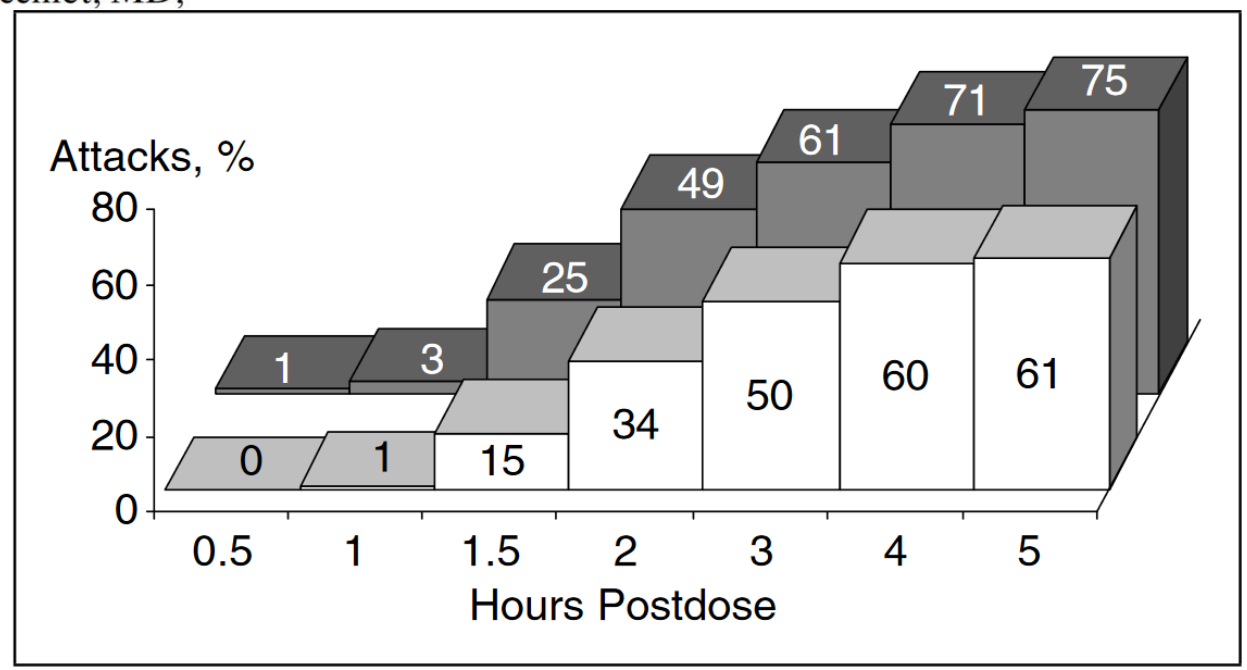

Fig 1.—Pain-free response rates, without use of rescue medication, in the total number of attacks. $P < .05$ between drugs. ■, IndoProCaf (indomethacin, prochlorperazine, and caffeine) (n = 175); □, sumatriptan (n = 175).

(*Headache* 2003;43:835-844)

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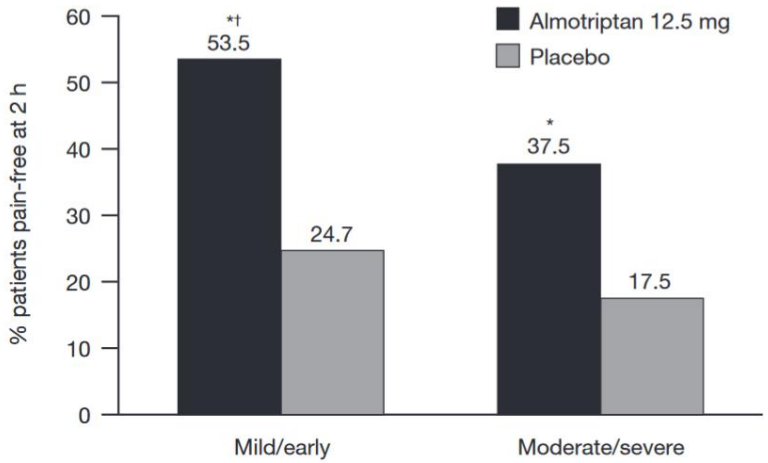
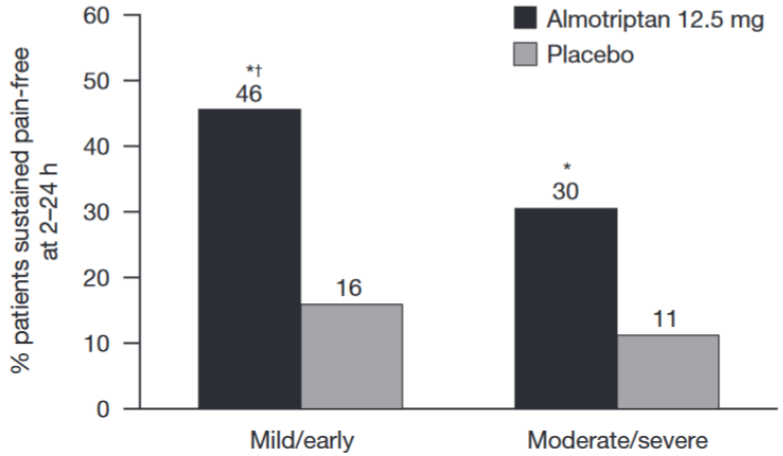
Reviews

The 'Act When Mild' (AwM) Study: A Step Forward in Our Understanding of Early Treatment in Acute Migraine

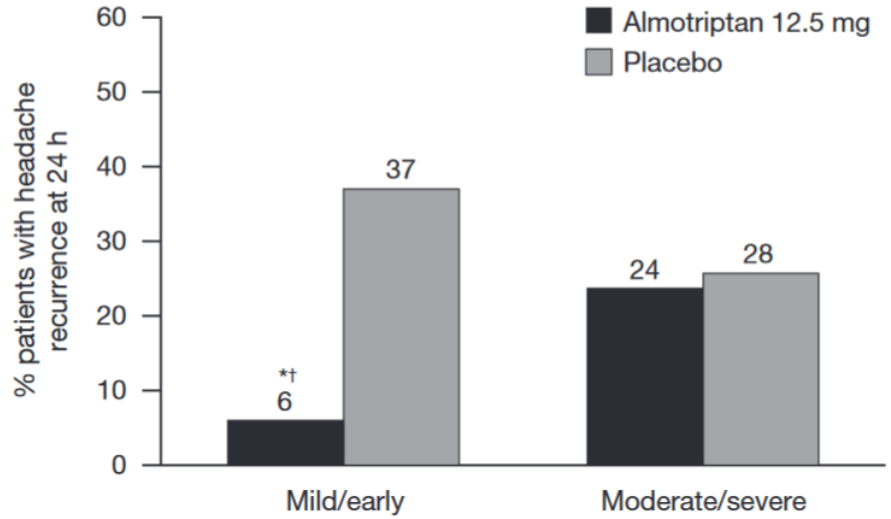
PJ Goadsby



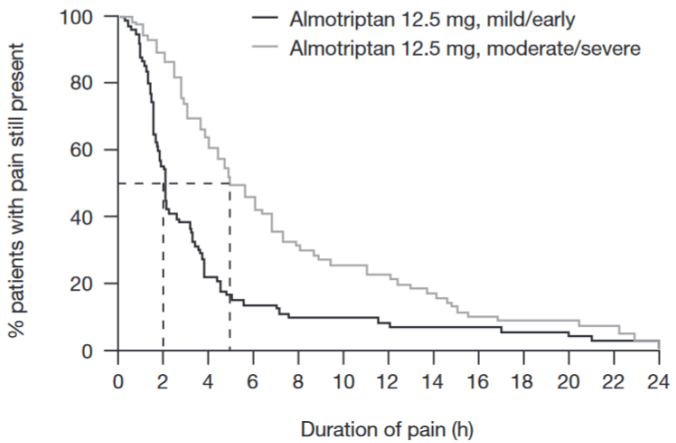
*$p \leq 0.001$ vs. placebo; †$p = 0.02$ vs. almotriptan moderate/severe



*$p < 0.002$ vs. placebo; †$p = 0.024$ vs. almotriptan moderate/severe



*$p = 0.0006$ vs. placebo; †$p = 0.0124$ vs. almotriptan moderate/severe



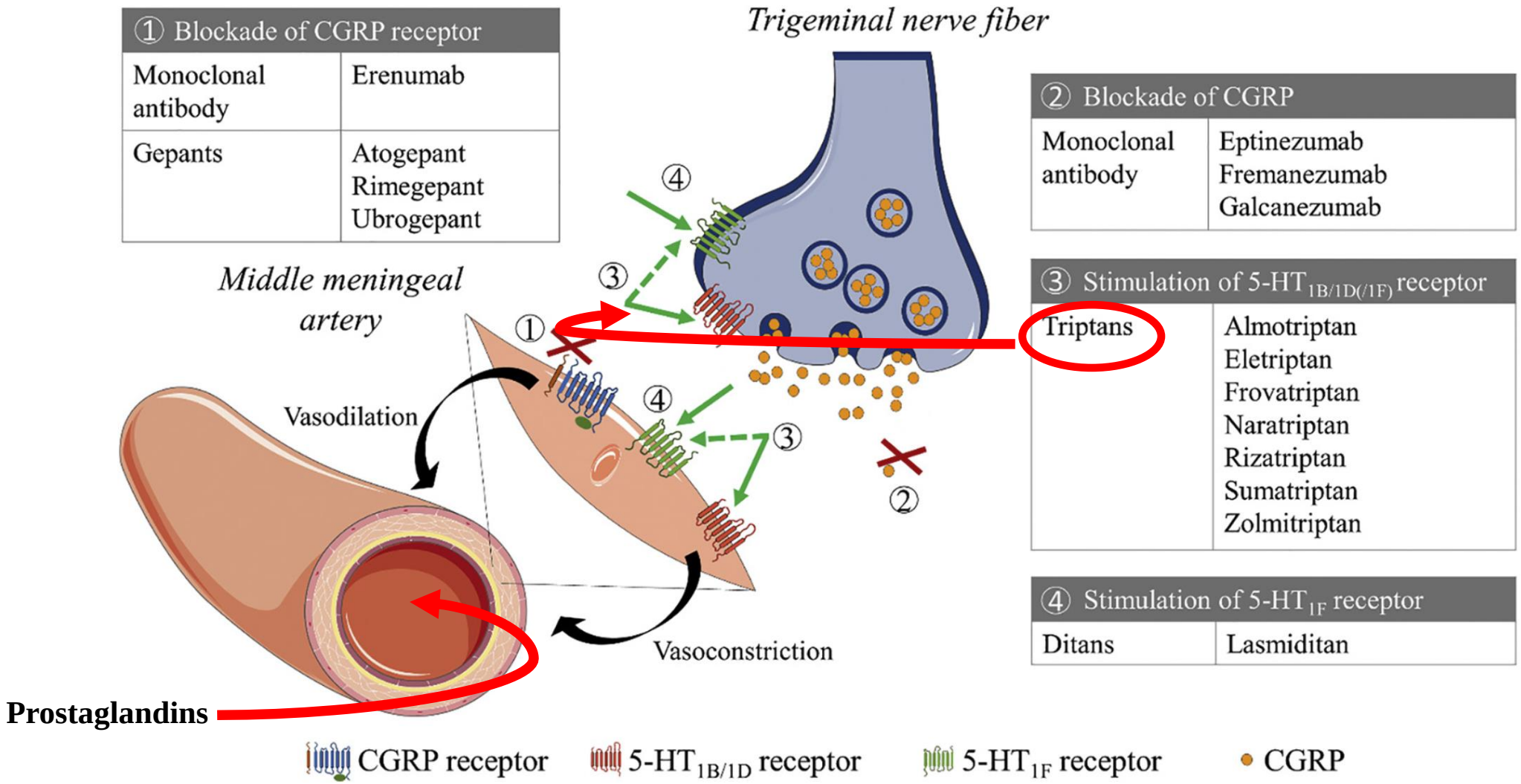


Fig. 1. Overview of migraine-specific medications and their possible targets. Migraine drugs can act through blockade of CGRP or its receptor or by stimulation of 5-HT$_{1B/1D/1F}$ receptors.

Thanks for your kind attention

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