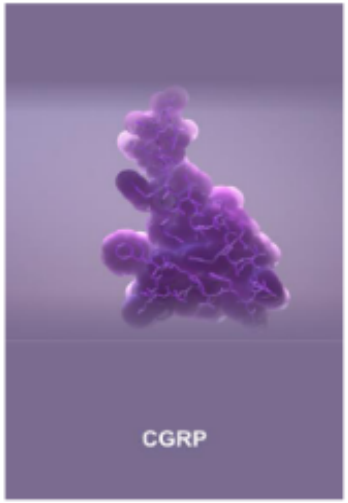
Diagnosis & Management of Migraine in Ten Steps

ZAHRA VAHABI

AGUSTE 2021

Calcitonin gene-related peptide (CGRP)

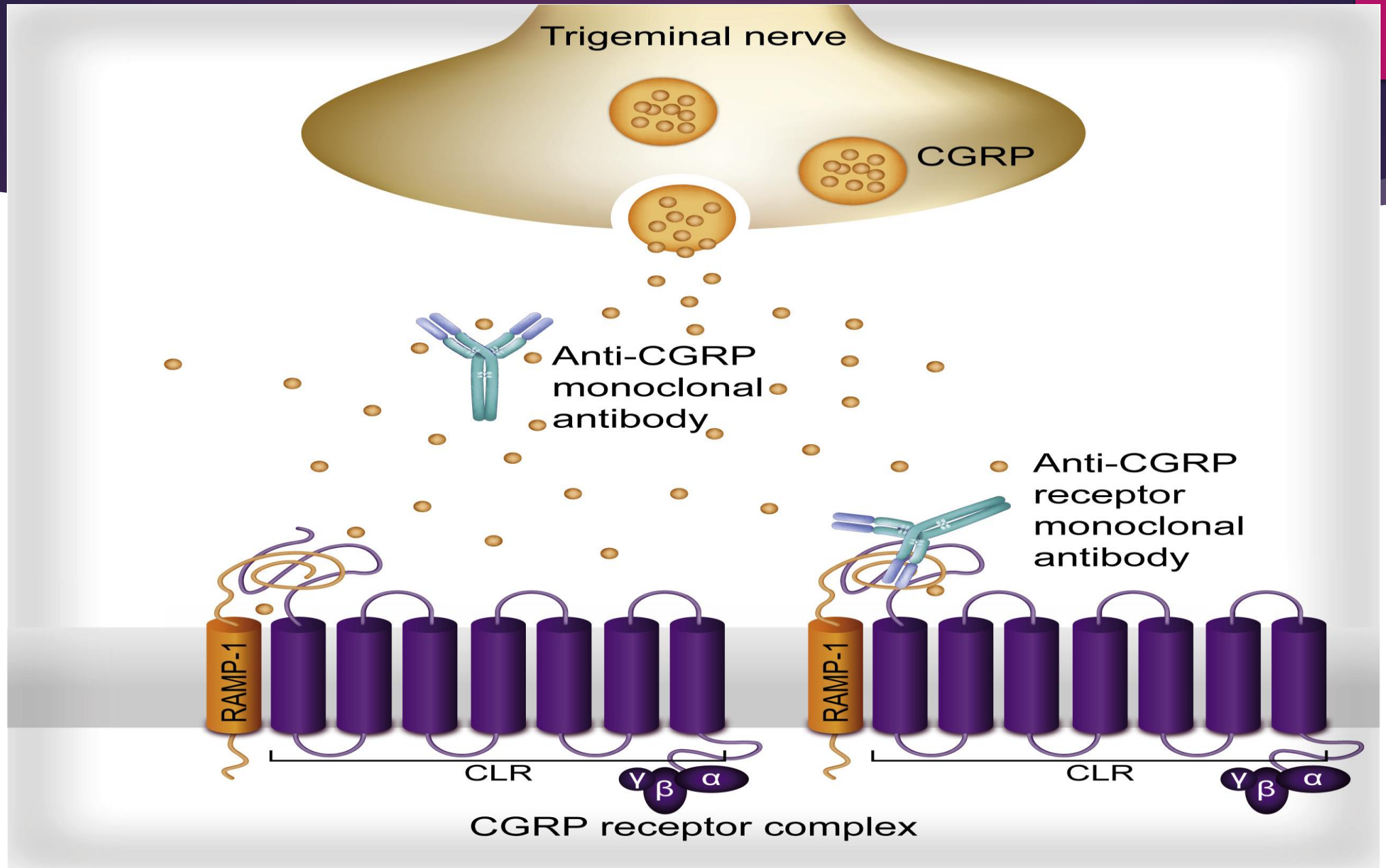
- Chromosome 11
- 37-amino-acid neuropeptide
- 2 isoforms
  - α-CGRP (central and peripheral nervous system)
  - β-CGRP (enteric nervous system)
- Coexists and interacts with neurotransmitters (SP, NKA, NPY, VIP etc.)
- In mammalian plasma, the half-life (T1/2) of CGRP is ~ 10 min



CGRP distribution in PNS and CNS

- Immunohistochemistry: mainly produced in cell bodies of both ventral and dorsal root neurons
- In C fibers and Aδ fibers
- Radioimmunology: especially common in trigeminal system (up to 50% of neurons produce CGRP)
- In perivascular fibers → major source of plasma CGRP
- In cortex, brain stem (locus coerulens, etc.), thalamus, cerebellum
- In glia cells

- CGRP can trigger a cascade of inflammatory mediators that feed into the trigeminovascular system.


Trigeminal nerve
CGRP
Anti-CGRP monoclonal antibody
Anti-CGRP receptor monoclonal antibody
RAMP-1
RAMP-1
CLR
CLR
γ
β
α
γ
β
α
CGRP receptor complex

Monoclonal antibodies targeting CGRP pathway

	Erenumab	Fremanezumab	Galcanezumab	Eptinezumab
Compound	AMG 334	LBR-101	LY2951742	ALD403
Target	Receptor	Ligand	Ligand	Ligand
Type	Human (100% human)	Fully humanized (>95% human)	Humanized (>90% human)	Humanized (>90% human)
Route of administration	Subcutaneous	Subcutaneous	Subcutaneous	Intravenous
Dosing	Monthly	Monthly or quarterly	Monthly	Quarterly
Half life	21 days	32 days	~25–30 days	~32 days

Diagnosis

1 When to suspect migraine

- Recurrent headache of moderate to severe intensity
- Visual aura
- Family history of migraine
- Onset of symptoms at or around puberty

2 Diagnosis of migraine

- Record medical history
- Apply diagnostic criteria
- Consider differential diagnoses
- Examine patient to exclude other causes
- Use neuroimaging only when a secondary headache disorder is suspected

3 Patient centricity and education

- Provide appropriate reassurance
- Agree on realistic objectives
- Identify predisposing and/or trigger factors
- Follow strategy to individualize therapy according to symptoms and needs

Acute and preventative treatment

4 Acute treatment

First-line medication

- NSAIDs (acetylsalicylic acid, ibuprofen or diclofenac potassium)

Second-line medication

- Triptans
- When triptans provide insufficient pain relief, combine with fast-acting NSAIDs

Third-line medication

- Ditans
- Gepants

Adjunct medications for nausea and/or vomiting

- Prokinetic antiemetics (domperidone or metoclopramide)

5 Preventative treatment

- Recommended for patients adversely affected on ≥2 days per month despite optimized acute therapy

First-line medication

- Beta blockers (propranolol, metoprolol, atenolol, bisoprolol)
- Topiramate
- Candesartan

Second-line medication

- Flunarizine
- Amitriptyline
- Sodium valproate[a]

Third-line medication

- CGRP monoclonal antibodies[b]

6 Managing migraine in special populations

Older people

- Secondary headache, comorbidities and adverse events are all more likely
- Poor evidence base for all drugs in this age group

Children and adolescents

- Be aware that presentation can differ from migraine in adults
- Parents and schools have important roles in the management of young children
- Bed rest alone can be sufficient
- Use ibuprofen for acute treatment and propranolol, amitriptyline or topiramate for prevention

Women who are pregnant or breastfeeding

- Use paracetamol for acute treatment
- Avoid preventive treatment if possible

Women with menstrual migraine

- Perimenstrual preventive therapy with long-acting NSAID or triptan

Clinical management and follow-up

7 Evaluation of treatment response and management of failure

- Use headache calendars
- Assess effectiveness and adverse events
- When outcomes are suboptimal, review diagnosis, treatment strategy, dosing and adherence
- When treatment fails, re-evaluate before changing
- Referral to specialist care should be reserved for patients whose condition is diagnostically challenging, difficult to treat or complicated by comorbidities

8 Managing complications

- Discourage medication overuse and recognize and stop established medication overuse to prevent MOH
- For MOH, withdraw overused medication, preferably abruptly
- Specialist referral is indicated for patients with chronic migraine
- Use preventive treatment for chronic migraine: topiramate, onabotulinumtoxinA or CGRP monoclonal antibodies[b]

9 Recognizing and managing comorbidities

- Identify comorbid conditions
- Select drugs and adjust their use according to comorbidities present
- Alleviate comborbidities if possible to improve outcome

10 Planning long-term follow-up

- Manage migraine long-term in primary care
- Repatriate patients from specialist care in a timely manner and with a comprehensive treatment plan
- Maintain stability of effective treatment in primary care and react to change

Box 2 | Diagnostic aids and screening tools

Headache diary

Headache diaries are useful diagnostic aids and can also, if needed, assist with re-evaluation of diagnosis at follow-ups (see Related links for an example headache diary).

Headache calendar

Headache calendars are useful in follow-ups for recording the temporal occurrence of headaches and related events, such as menstruation (see Related links for an example headache calendar).

Three-item Identify Migraine questionnaire

The three-item Identify Migraine (ID-Migraine) questionnaire identifies individuals who are likely to have migraine on the basis of their answers to three questions regarding headache-associated nausea, photophobia and disability[22].

Migraine Screen Questionnaire

The Migraine Screen Questionnaire (MS-Q), like ID-Migraine, is designed to screen patients for migraine but includes five questions regarding headache frequency, intensity and length, headache associated nausea, photophobia and phonophobia, and disability[23].