We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,300

Open access books available

172,000

International authors and editors

190M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Introductory Chapter: Migraine in Post-Triptan Era: New Therapeutic Horizons

Wojciech Kozubski and Izabela Domitrz

1. Introduction

Migraine is described as a chronic, most probably genetically determined disease, in vast majority of patients characterized by the occurrence of headache attacks. The bouts of headache are accompanied by specific symptoms and signs as nausea—in majority of patients and vomiting—in almost half of them, as well as photophobia and phonophobia [1]. Since they left untreated, the attacks last—in adult patient—from 4 hours up to 3 days. The onset of the disease falls between 18 and 35 years and migraine is regarded as a life-long condition, however it may present a different clinical face in different period of patient's life as far as frequency and severity of the attacks are concerned. In general, migraine is more than twice more common in adult women (approx. 15% of general population) than in adult men—roughly 6% of the population [2], especially in the period of highest occurrence. However, relations and proportions might be entirely different in childhood and senescence—approximately the same percentage of young boys suffer from migraine as girls [3] and the disease is almost three times more common among elderly men than postmenopausal women [4].

The vast majority of the patients usually experience the moderate and/or severe pain intensity during attacks. It results in the fact that almost three-quarters of migraine victims present highly diminished effectiveness during disease attack [5]. It means the effective treatment of each single attack plays a decisive role in the reduction of both biological (i.e. pain, accompanying symptoms), social and economic aspects of the disease.

2. Triptans

For a long time specific and selective 5-HT_{1B/1D} receptor agonists—a class of drugs called triptans (including sumatriptan, zolmitriptan, naratriptan, rizatriptan, almotriptan, eletriptan, and frovatriptan)—have been used as an effective and relatively safe measures against migraine attacks, regarded as almost the drugs of choice in migraine episodes [6, 7]. The drugs were especially recommended in patients with attacks poorly responded to NSAIDs or in whom NSAIDs were contraindicated. What is more—the fewer side effects were associated with triptans than in other anti-migraine drugs, and triptans were more effective at aborting migraine bouts [8]. However, during the years of triptan administration, it was noticed, that these group of drugs, even used in proper dose and manner are ineffective in some 16–18% of migraine victims [9]. What is more the side effects of triptans

(coronary-like pain symptoms) appeared dangerous and strictly unacceptable for quite a percentage of patients [10]—in fact, triptans are contraindicated in most cardiovascular diseases. In these situation the strong need of new—effective and especially cardiac—safe migraine killers—became obvious.

3. After triptans

The next selective drugs tried in abortive treatment in migraine were ditans—a class of molecules that selectively bind to 5-HT_{1F} receptors. The ditans are not encountered in vessels, being widespread in CNS, especially in brain stem, hampering the increased trigeminal system activity during migraine attack [11]. After the years of clinical studies, one of these molecules—lasmiditan, after first—relatively positive trials [12]—finally—has been approved by the FDA for the acute treatment of migraine with or without aura in adults [13].

Also the next seemingly promising group—gepants, calcitonin-gene related peptide (CGRP) receptor antagonist—after first enthusiastic results concerning the efficacy of the first generation of antagonist—telcagepant [14] or ubrogepant [15], were the subject of more detailed debates and considerations. The main reason for the doubts was their accented hepatotoxicity [16]. Eventually, the FDA has approved an orally disintegrating tablet formulation of rimegepant [17], that was the second, after ubrogepant, oral drug of this group, available in anti-migraine armamentarium. We still waiting for the final results and the potential approval of the next two molecules from second gepants generation, i.e. atogepant, vazegepant.

4. Monoclonal antibodies against CGRP and the CGRP receptor as new-generation drugs for migraine treatment

Monoclonal antibodies (mAbs) developed against CGRP receptor (as erenumab) or CGRP molecule itself (namely—fremanezumab, galcanezumab, and eptinezumab) were the next big hope in therapeutic attitude to migraine. The drugs of these group exert strong inhibiting effect on CGRP release during migraine attack, thus hampering its vasodilative effect [18, 19]. The results of many registered pharmacoclinical studies/trials showed both effectiveness and safety of these drugs, that reduced both the number of migraine episodes, days with headache and administration of acute headache killers per month in migraineurs. The next advantages of these group were very convenient, patient-friendly dose regimen (once a four weeks) and—as it looks now—the absence of serious side effect [20, 21]. It seems that relatively fast onset of action (in the first month of implementation), high efficacy, and good tolerability make this class of drugs the real revolution in migraine treatment [22, 23] compared with that of ergotamine introduction (in 1927) or the first triptans in 1990. In fact, they are the second characteristic molecule—after methysergide—targeting the most specific mechanism of migraine attacks. This group of drugs showed effectiveness both in episodic and chronic migraine—and what is more, also, in migraine-like episodes in patients with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), that is quite a phenomenon [24].

We do hope that in time and gaining more experience with these group of antimigraine drugs, monoclonal antibodies against CGRP complex will become the first-line treatment of the disease.

IntechOpen

Author details

Wojciech Kozubski^{1*} and Izabela Domitrz²

¹ Department of Neurology, Charles Marcinkowski University of Medical Sciences in Poznan, Poland

² Department of Neurology, Faculty of Medical Sciences, Medical University of Warsaw, Poland

*Address all correspondence to: wkozubski@ump.edu.pl

IntechOpen

© 2020 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

References

- [1] Ludwig J, Bartsch T, Wasner G, Baron R. Autonomic dysfunction in migraines. In: Olesen J, Goadsby P, Ramadan NM, Tfelt-Hansen P, Welch KMA, editors. *The Headaches*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2006. pp. 377-384
- [2] Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2007;**68**:343-349
- [3] Rasmussen BK. Epidemiology of migraine. In: Olesen J, Goadsby P, Ramadan NM, Tfelt-Hansen P, Welch KMA, editors. *The Headaches*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2006. pp. 235-242
- [4] Prencipe M, Gasini AR, Ferretti C. Prevalence of headache in an elderly population: Attack frequency, disability, and use of medication. *J Neurol Neurosurg Psychiatry*. 2001;**70**:377-381
- [5] Edmeads J, Mackell JA. The economic impact of migraine: An analysis of direct and indirect costs. *Headache*. 2002;**42**:501-509
- [6] Goadsby PJ. Serotonin 51B/1D receptor agonists in migraine. *CNS Drugs*. 1998;**10**:271-286
- [7] Lipton RB, Bigal ME, Rush SR, Yenkosky JP, Liberman JN, Bartleson JD, et al. Practice patterns among neurologists. *Neurology*. 2004;**62**:1926-1931
- [8] Cameron C, Shannon K, Shu-Ching H, Murphy M, et al. Triptans in the Acute Treatment of Migraine: A Systematic Review and Network Meta-Analysis. *Headache*. 2015;**55**(Suppl. 4): 221-235
- [9] Ferrari MD. Migraine. *The Lancet*. 1998;**351**:1043-1051
- [10] Thorlund K, Mills EJ, Wu P, Ramos E, Chatterjee A, Druyts E, et al. Comparative efficacy of triptans for the abortive treatment of migraine: A multiple treatment comparison meta-analysis. *Cephalalgia*. 2014;**34**:258-267
- [11] Jamieson DG. The safety of triptans in the treatment of patients with migraine. *The American Journal of Medicine*. 2002;**112**:135-140
- [12] Vila-Pueyo M, Strother L, Page K, et al. Lasmiditan inhibits trigeminovascular nociceptive transmission. *Cephalalgia*. 2016;**36**:152
- [13] <https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-patients-migraine>.
- [14] Farkkila M, Diener HC, Geraud G, et al. Efficacy and tolerability of lasmiditan, an oral 5-HT_{1F} receptor agonist, for the acute treatment of migraine: A phase 2 randomized, placebo-controlled, parallel-group, dose-ranging study. *Lancet Neurology*. 2012;**11**:405-413
- [15] Ho TW, Ferrari MD, Dodick DW, et al. Efficacy and tolerability of MK-0974 (telcagepant), a new oral antagonist of calcitonin gene-related peptide receptor, compared with zolmitriptan for acute migraine: A randomized, placebo-controlled, parallel-treatment trial. *Lancet*. 2008;**372**:2115-2123
- [16] Voss T, Lipton RB, Dodick DW, et al. A phase IIb randomized, double-blind, placebo-controlled trial of ubrogepant for the acute treatment of migraine. *Cephalalgia*. 2016;**36**:887-898
- [17] Rimegepant (Nurtec ODT) for Acute Treatment of Migraine. *Journal of the American Medical Association*. 2020;**324**(9):890-891. DOI: 10.1001/jama.2020.8493

[18] Moreno-Ajona D, Perez-Rodriguez A, Goadsby PJ. Gepants, calcitonin-gene related peptide (CGRP) receptor antagonist: What could be their role in migraine treatment. *Current Opinion in Neurology*. 2020;**33**:309-315

[19] Russo AF. Calcitonin gene-related peptide (CGRP): A new target for migraine. *Annual Review of Pharmacology and Toxicology*. 2015;**55**:533-552

[20] Moskowitz MA. Pathophysiology of headache – Past and present. *Headache*. 2007;**47**(suppl. 1):S58-S63

[21] Sun H, Dodick DW, Silberstein S, et al. Safety and efficacy of AMG 334 for prevention of episodic migraine: A randomized, double-blind, placebo-controlled, phase 2 trial. *Lancet Neurol*. 2016;**15**:382-390

[22] Silberstein SD, Dodick DW, Bigal ME, et al. Fremanezumab for the preventive treatment of chronic migraine. *The New England Journal of Medicine*. 2017;**377**:2113-2122

[23] Skljarevski V, Oakes TM, Zhang Q, et al. Effect of different doses of galcanezumab vs placebo for episodic migraine prevention: A randomized clinical trial. *JAMA Neurology*. 2018;**75**:187-193

[24] Goldstein ED, Badi MK, Meschia JM. Treating chronic migraine in CADASIL with calcitonin gene-related peptide receptor antagonism. *Neurology Clinical Practice*. 2019. DOI: <https://doi.org/10.1212/CPJ.0000000000000651>