CGRP ANTAGONISTS AND THE TREATMENT OF MIGRAINE – NEW HEROES AGAINST AN OLD ENEMY

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Migraine is one of the most common neurological diseases and about 20% of patients suffer from frequent episodic or chronic forms of the disease, which represent a significant global cause of chronic disability. Despite its high prevalence, the pathophysiology of migraine is still not completely understood. However, it has been known for several decades that the development of migraine attacks is dependent on the calcitonin gene-related peptide (CGRP), a neuropeptide that modulates nociceptive signaling within neuronal pathways important for migraine pain. Drugs that reduce the effects of CGRP (CGRP antagonists) have recently become available and include small-molecule CGRP-receptor antagonists (so-called gepants) that are approved for acute treatment and/or prevention of migraine attacks (ubrogepant, atogepant, rimegepant), as well as monoclonal antibodies, which are approved for prevention of migraine attacks (anti-CGRP antibodies: fremanezumab, galcanezumab, eptinezumab; anti-CGRP receptor antibody: erenumab). The effectiveness of gepants in alleviating migraine attacks is somewhat lower compared to triptans (standard drugs for treating migraine attacks), but gepants are considered safer than triptans with regard to cardiovascular side effects and the risk of medication-overuse headache. Monoclonal anti-CGRP antibodies have been shown to be useful drugs for patients who have not responded to standard prophylactic therapy (e.g., β-blockers or antiepileptics), but their high cost limits widespread use. Although the effectiveness of CGRP antagonists has been unequivocally proven, it will take time to precisely define the role of these drugs in modern migraine pharmacotherapy, and it is especially important to examine the safety of their long-term use.

References

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Acknowledgements

This work was funded by the Ministry of Education, Science and Technological Development, Republic of Serbia through Grant Agreement with University of Belgrade-Faculty of Pharmacy No: 451-03-68/2022-14/200161.

CGRP ANTAGONISTI I TERAPIJA MIGRENE – NOVI HEROJI PROTIV STAROG NEPRIJATELJA

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Migrena spada u najčešća neurološka oboljenja i oko 20% pacijenata ima čestu epizodičnu ili hroničnu formu bolesti, koje predstavljaju značajan uzrok hronične onesposobljenosti na globalnom nivou. Uprkos visokoj prevalenciji, patofiziologija migrene je još uvek nedovoljno razjašnjena. Međutim, već nekoliko decenija je poznato da u nastanku napada migrene veliku ulogu igra peptid srodan kalcitoninu (engl. *calcitonine gene related peptide* – CGRP), neuropeptid koji moduliše nociceptivnu signalizaciju u okviru neuronskih puteva značajnih za nastanak migrenoznog bola. Lekovi koji smanjuju efekte CGRP-a (CGRP antagonisti) su nedavno postali dostupni i obuhvataju antagoniste CGRP-receptora male molekulske mase (tzv. gepanti) koji su odobreni za akutni tretman i/ili prevenciju napada migrene (ubrogepant, atogepant, rimegepant), kao i monoklonska antitela koja su odobrena za prevenciju napada (anti-CGRP antitela: fremanezumab, galkanezumab, eptinezumab; anti-CGRP receptorsko antitelo: erenumab). Efikasnost gepanta u ublažavanju napada migrene je nešto niža u poređenju sa triptanima (standardnim lekovima za tretman napada), međutim smatra se da su gepanti bezbedniji od triptana u pogledu kardiovaskularnih neželjenih efekata i rizika od izazivanja glavobolje prekomerne upotrebe analgetika. Monoklonska anti-CGRP antitela su se pokazala kao korisni lekovi za pacijente koji nisu odgovorili na standardnu profilaktičku terapiju (npr. β-blokatorima ili antiepilepticima), međutim visoka cena ograničava njihovu širu upotrebu. Iako je efikasnost CGRP antagonista nesumnjivo dokazana, za precizno definisanje uloge ovih lekova u savremenoj farmakoterapiji migrene će biti potrebno vreme, a posebno značajno je ispitati bezbednost njihove dugoročne primene.

Literatura

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Zahvalnica

Ovaj rad je finansiran od strane Ministarstva prosvete, nauke i tehnološkog razvoja Republike Srbije kroz Ugovor sa Univerzitetom u Beogradu-Farmaceutskim fakultetom broj: 451-03-68/2022-14/200161.